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BLOOD SUPPLY OF THE NERVES OF THE UPPER LIMB IN MAN

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Investigations on the blood supply of peripheral nerves by Quénu and Lejars[1] (1890, 1892), Bartholdy[2] (1897) and Tonkoff[3] (1898, 1907), toward the close of the last century, extended the rather limited observations previously made by Haller[4] (1756), Isenflamm and Doerffler[5] (1768), Bichat[6] (1830) and Hyrtl[7] (1859, 1864) and culminated in the publication of a series of papers which made available a considerable body of accurate information on this subject. It is perhaps unfortunate that these reports appeared at a time when interest in the peripheral nervous system was dominated by the problems of degeneration and regeneration and by the behavior of the apparently more active elements of the nerve in those processes, namely, the axis-cylinder and its myelin and Schwann sheaths. As a result, any possible effect of the blood supply on axonal conduction, degeneration and repair failed to attract attention, though suggestions that occlusion of the vasa nervorum might be responsible for certain disorders of peripheral nerve function did appear from time to time in the literature (Lapinsky,[8] 1899, and others). Thus, in 1907 Tonkoff[3b] was drawn to protest:

> . . . den Arterien der Nerven bis jetzt zu wenig Beachtung geschenkt worden ist; in den Lehr- und Handbüchern werden sie meist ganz übergangen oder doch nur oberflächlich erwähnt.

Even as late as the great war of 1914 to 1918, when extensive investigations were undertaken for the purpose of extending knowledge of nerve structure and nerve function as a basis for improvement in the diagnosis and treatment of the nerve injuries which had accumulated in such large numbers, the possibility that the vasa nervorum might be implicated failed to arouse much interest.

There are signs, however, that this defect is being remedied. In 1926 Ramage,[9] unaware of the contributions of Tonkoff and of Bartholdy, reexamined, in the light of the observations of Quénu and Lejars, the blood supply to the large peripheral nerves of the upper limb in man. The present world conflict has given a new impetus to the study of peripheral nerve injuries; physiologists are now appreciating the functional significance of the blood supply to nerves, while the consequences of pathologic changes in the vasa nervorum are not being neglected. The observations of Quénu and Lejars, Tonkoff, Bartholdy and Ramage on the anatomic features of the vasa nervorum, however, remain the most informative and accurate available.

Studies on peripheral nerve injuries at a military hospital in Australia have inevitably introduced problems requiring for their solution precise knowledge concerning neurovascular relationships. Reference to the relevant literature has shown that previous investigations failed to provide certain essential details relative to the arterial supply of individual nerves. Moreover, the material used in the earlier work was predominantly fetal in type, and this suggested that a more extensive investigation into the supply to individual nerves in a larger series of adult arms was desirable in order to determine whether postnatal changes in any way modify the extraneural and intraneural distribution of the vasa

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1. Quénu, J., and Lejars, F.: (*a*) Les artères et les veines des nerfs, Compt. rend. Acad. d. sc. **111**: 608, 1890; (*b*) Étude anatomique sur les vaisseaux sanguins des nerfs, Arch. de neurol. **23**:1, 1892.

2. Bartholdy, K.: Die Arterien der Nerven, Morphol. Arb. **7**:393, 1897.

3. Tonkoff, V. N.: (*a*) Die Arterien der Intervertebralganglien und der Cerebrospinalnerven des Menschen, Internat. Monatschr. f. Anat. u. Physiol. **15**:353, 1898; (*b*) Die nervenbegleitenden Gefässnetze beim Embryo und die Arteriae nutriciae nervorum beim Erwachsenen, Anat. Anz. **30**:471, 1907.

4. Haller, A.: Icones anatomicae, Göttingen, A. Vandenhoeck, 1756.

5. Isenflamm, J. F., and Doerffler, J. F.: De vasis nervorum, Erlangen, 1768.

6. Bichat, M. F. X.: General Anatomy, London, 1830, vol. 1, p. 168.

7. Hyrtl, J.: (*a*) Oesterr. Ztschr. f. prakt. Heilk., 1859; cited by Tonkoff[3b]; (*b*) Denkschr. d. math.-nautrw. Cl. d. k. Akad. d. Wissensch., 1864, p. 23; cited by Tonkoff.[3b]

8. Lapinsky, M.: Ueber Veränderungen der Nerven bei acuter Störung der Blutzufuhr, Deutsche Ztschr. f. Nervenh. **15**:364, 1899; cited by Adams.[10]

9. Ramage, D.: The Blood Supply to the Peripheral Nerves of the Superior Extremity, J. Anat. **61**:198, 1927.

nervorum. It may be mentioned here that the results of the present study indicate that there are no postnatal changes of any significance in the vascular pattern. For the purpose of checking the observations of earlier investigators and of extending them wherever possible in terms of modern requirements, the normal distribution of the vasa nervorum has been reinvestigated in a larger series of adult arms than has hitherto been examined. It is not proposed in this report to review in any detail the literature on the subject. This has recently been covered in an excellent review by Adams [10] (1942), whose paper also contains a comprehensive bibliography.

MATERIAL AND METHODS

Observations were made on the blood supply of the median, ulnar and radial nerves in adult human arms by means of the following methods:

1. The extraneural features of the vasa nervorum to all three nerves were investigated by dissection in 37 adult arms. An examination of the pattern in both arms in 8 subjects permitted a comparison of the disposition of the vessels on the two sides; the remaining 21 arms were unpaired. In each nerve the blood supply was examined from the origin of the nerve in the axilla to the distal border of the flexor retinaculum.

2. The intraneural vascular pattern was studied macroscopically and microscopically.

(*a*) Macroscopic study: The pattern was outlined by intra-arterial injection of colored gelatin or india ink in limbs freshly amputated for conditions not affecting the blood vessels or nerves. After the injection the nerves were dissected, removed, dehydrated and cleared in cedar-wood oil. The intraneural pattern was then traced by direct observation and microdissection.

(*b*) Microscopic study: (1) After examination of the extraneural relations in the 37 specimens the nerves were removed and studied histologically. Ten segments, each 1 cm. in length, were cut from the median and the ulnar nerve. The first segment was taken in the axilla; the fifth, at the elbow, and the tenth, at the wrist. Of the remaining segments, the second, third and fourth were evenly spaced between the axilla and elbow, and the sixth, seventh, eighth and ninth, between the elbow and the wrist. In view of the large number of vessels usually reaching the ulnar nerve in the neighborhood of the medial epicondyle, this nerve was sectioned not only in the groove but immediately above and below it. In the case of the radial nerve, segments were taken from the axilla, at the entrance to the spiral groove, in the groove and in the muscular furrow between the brachioradialis and the brachialis muscle. The fifth, and last, section included the terminal portion of the nerve and the first parts of the posterior interosseous and superficial radial nerves.

Each segment was fixed in the usual manner and embedded in paraffin. The transverse sections, 15 microns in thickness, were cut from each block and stained with hematoxylin and eosin. This material gave valuable information concerning the size, type and disposition of the vessels in different nerves and at different levels of the same nerve.

(*2*) The intraneural pattern was also studied by examining transverse and longitudinal sections of fresh nerves, cut at 250 microns, in which the vessels had been outlined by Pickworth's sodium nitroprusside method.

(3) Additional information concerning the intraneural pattern was obtained from the examination of transverse and longitudinal sections, 250 microns in thickness, of the injected nerves.

10. Adams, W. E.: The Blood Supply of Nerves: I. Historical Review, J. Anat. **76**:323, 1942.

NOMENCLATURE

In order to avoid any confusion concerning the terminology employed in describing the histologic features of the nerve and its contained vessels, it is proposed to outline briefly the nomenclature employed in this investigation.

The Vessels.—The structure, and not the size, of the vessel was used as the sole basis for classification. The lumen of a vessel can be modified so readily by physical and chemical agencies and is subject to so many variations during life that its size was disregarded.

A capillary is defined as a vessel in which endothelium is the sole component of the vessel wall. This endothelium is not folded.

A precapillary, or precapillary arteriole, is lined with a layer of unfolded endothelium, outside which is a simple, thin circular coat of smooth muscle, one to two cells in thickness.

An arteriole has a wall composed of three recognizable layers. The lumen is lined with endothelium, external to which is an internal elastic membrane. Owing to the presence of this elastic layer, the lumen is irregularly folded. The intermediate layer, or tunica media, is composed predominantly of smooth muscle. The most external layer, or tunica adventitia, is composed of fine fibroelastic tissue. It is thin and ill defined and merges without any sharp line of demarcation into the surrounding connective tissue. With the exception of the median artery, no vessels larger than arterioles have been seen in the sections of the nerves examined.

The postcapillary venules which drain the capillaries have in general thinner walls than the corresponding precapillary arterioles, while, in addition, the smooth muscle coat is absent. In the larger adjoining venules the wall is very thin in relation to the size of the lumen and is composed principally of connective tissue with a trace of smooth muscle. The large lumen, the very thin wall and the predominance of connective tissue in the wall are readily identifiable features.

The Nerve.—The intraneural disposition of the vessels is best expressed in terms of the internal architecture of the nerve. The nomenclature used is illustrated in figure 1 *A*. The individual nerve fibers are collected into fasciculi, oval or circular on transverse section, each of which is surrounded by a ring of dense white fibrous connective tissue. This is the perineurium,

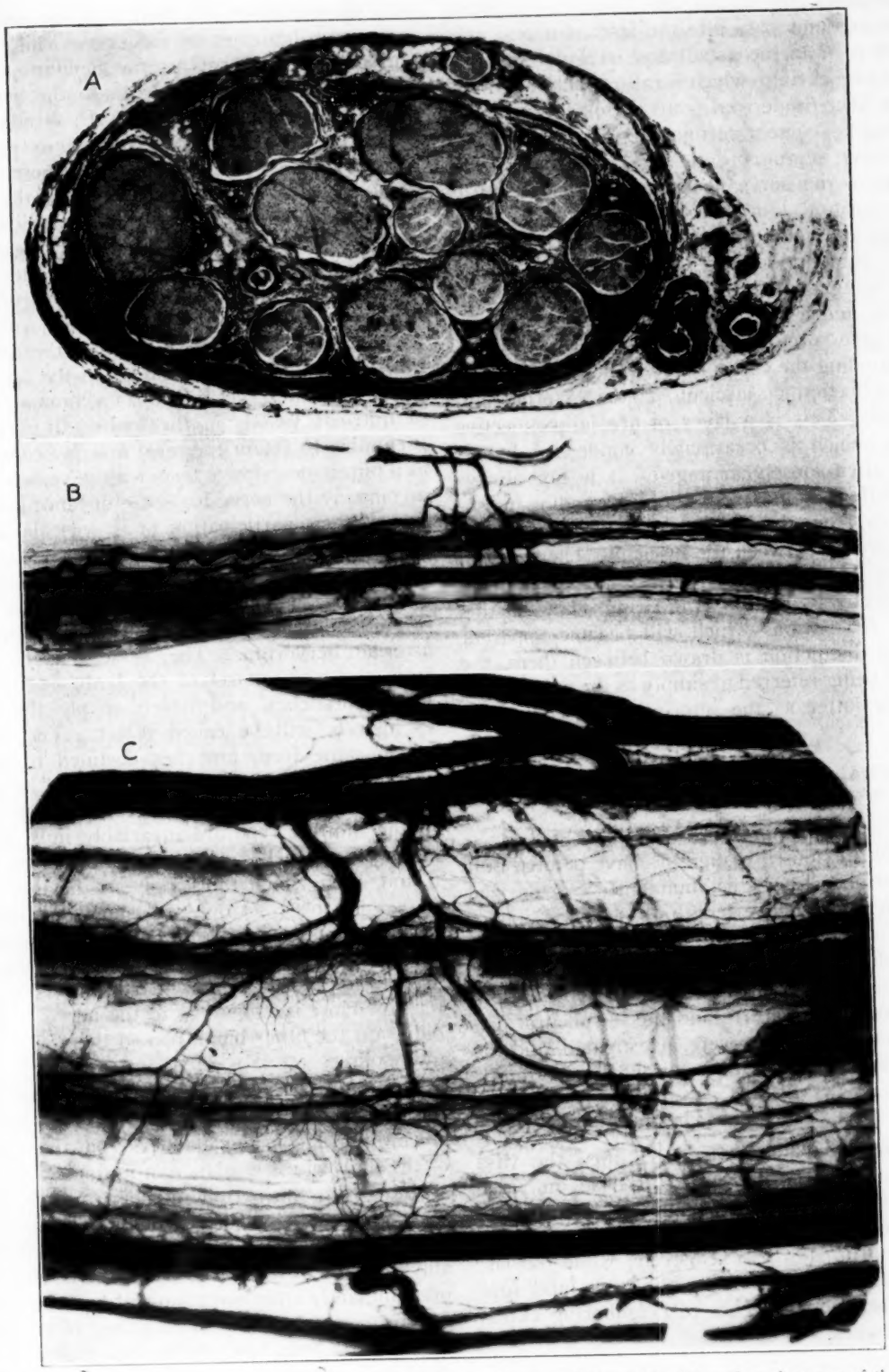

Fig. 1.—*A*, transverse section of the median nerve in the forearm, illustrating the various features of the internal architecture of the nerve. Note the thickness of the intrafascicular connective tissue septums and the position of the median artery and intraneural vessels. *B*, photomicrograph of an injected specimen; × 5. Note the relation of the arterioles and venules to one another at the site of entry into the nerve and the coarser features of their distribution within the nerve. *C*, photomicrograph of an injected specimen, demonstrating the intraneural vascular plexus; × 22.

or perifascicular sheath, and from it connective tissue septums pass into the fasciculus and subdivide it in an inconstant and irregular manner. The endoneurium, which sheathes each individual nerve fiber, is derived from these septums. According to current terminology, both the intrafascicular septums and the connective tissue sheath of the nerve fiber are to be classified as endoneurium. However, these septums are often thicker and composed of coarser fibers than the tissue surrounding the individual nerve fibers. They bring about a further refinement of the fiber pattern, and when the fasciculi divide they do so along the preformed intrafascicular septums. Surrounding the entire nerve, which is composed of a collection of fasciculi, is the external epineurium. This is a layer of areolar connective tissue, which is occasionally condensed but is more often loosely arranged. It is not always well differentiated from the surrounding mesoderm or from the open areolar tissue (internal epineurium) between the fasciculi. The external and the internal epineurium are usually referred to collectively as the epineurium, but in this paper, for reasons which will become apparent later, a distinction is drawn between them, the former being referred to simply as the epineurium and the latter as the interfascicular connective tissue.

GENERAL FEATURES OF THE EXTRANEURAL AND INTRANEURAL VASCULAR PATTERNS

As all previous investigators have pointed out, each peripheral nerve is abundantly vascularized throughout its entire length by a succession of vessels, the vasa nervorum, which, by their repeated division and anastomosis within the nerve, form an unbroken intraneural vascular net. Both the extraneural features and the intraneural disposition of the vessels were investigated, and the results in each case will be discussed separately.

EXTRANEURAL PATTERN

Classification.—Tonkoff [3a] classified the vasa nervorum into two types: arteriae nutritiae nervorum and arteriae comitantes nervorum. According to this author, the former supply the nerve and its sheaths exclusively, while the latter, though they accompany the nerve and supply it, also send branches to neighboring extraneural tissues.

Such a classification requires modification. Tonkoff did not make it clear whether the arteriae comitantes, after coursing with the nerve, terminate in it or whether their supply is predominantly to the nerve or to extraneural tissues. If the vessel is concerned principally with the supply of extraneural tissues and sends only some branches to the nerve while accompanying it, the term arteria comitans nervi is appropriate, and the branches to the nerve become true arteriae nutritiae. If, on the other hand, the vessel supplies the nerve predominantly but sends branches elsewhere before finally penetrating and terminating in the nerve, it should be regarded as an arteria nutritia nervi. Tonkoff's classification, moreover, disregards the vessels which do not accompany a nerve but which send a branch or branches to it while on their way to other structures. Such vasa nervorum could not be regarded as either arteriae nutritiae or arteriae comitantes in the sense implied by Tonkoff, yet they form a common source of nutrient vessels in the limbs. It would be preferable to retain the term arteriae comitantes as a purely descriptive term for the vessels which accompany the nerve for some distance irrespective of their participation in its vascularization.

In this paper all the vessels which enter the nerve and terminate intraneurally will be regarded as nutrient arteries irrespective of their origin and will be referred to subsequently as arteriae nervorum. The vessels which come from the main vessel of the limb, or from its named branches, and which supply the nerve exclusively will be called direct. The vessels which come from branches destined to supply extraneural tissues predominantly will be called indirect. In the limbs the vessels giving origin to the indirect type are invariably muscular or cutaneous branches. Reference to tables 1, 2, 3 and 4, in which the supply to the individual nerves has been set out, will show that indirect nutrient vessels are not commonly present. Tonkoff [3a] agreed that it is rare for nutrient arteries to come from muscular branches no matter how close they may be to the nerve. Bartholdy,[2] on the other hand, named them as a common source.

Origin.—(*a*) All investigators are agreed that the arteriae nervorum to any one nerve are derived, in an inconstant manner, from the arteries of the limb which establish an intimate anatomic relation with the peripheral nerve or which, at most, are not far distant from it. Since gross neurovascular relations in the limbs are reasonably constant, each nerve comes to be supplied predominantly from a constant group of arteries, which may include the main artery of the limb, its named branches, unnamed muscular or cutaneous branches or an anastomotic arterial loop, such as is commonly present in the neighborhood of the elbow. Thus the ulnar nerve is accompanied throughout its course by a continuous vascular pathway, formed in turn by the axillary, brachial, ulnar collateral, supratrochlear,

posterior ulnar recurrent and ulnar arteries, and it is these vessels which provide the arteriae nervorum. If there is any departure from the normal arterial pattern, then the nerve is supplied from the nearest available channel.

It has been established in this investigation that for each individual nerve there is a reasonably constant group of arteries which, by nature of their anatomic disposition, are favorably situated to supply the nerve and from which the arteriae nervorum are consequently derived. Despite the presence of this reasonably constant vascular pathway, both the number and the precise origin of the arteriae nervorum arising from the vessels composing it vary considerably, as is well illustrated in the tables 1, 2, 3 and 4, setting out the extraneural supply to the individual nerves. Not only does the extraneural pattern vary from subject to subject, as has already been pointed out by Bartholdy, but the arrangement is also asymmetric on the two sides of the body. Nevertheless, it is important to keep in mind that these variations do occur along a reasonably constant vascular pathway.

All investigators, with the exception of Quénu and Lejars, have agreed on the inconstancy of the number and origin of the arteriae nervorum. This inconstancy is such a characteristic and obvious feature that it is perhaps conceivable that when Quénu and Lejars [1b] stated "chaque tronc nerveux reçoit ses artères d'origines constantes," they had in mind not a constant formula for the arteriae nervorum themselves, but a constant system of major vessels from which the nutrient arteries took origin in serial fashion down the arm. However, there is nothing definite in their account to support such an interpretation.

(*b*) Though the site of origin is variable, there are certain regions where nerves habitually receive nutrient arteries, such as at the elbow, in the case of the ulnar nerve, and in the spiral groove, in the case of the radial nerve.

(*c*) When several arteriae nervorum arise from any one vessel participating in the formation of the accompanying vascular chain, it is unusual to see their origins evenly spaced along the present artery. On occasion there is a tendency for clustering to occur at certain points on the nerve.

(*d*) Roux [11] established certain rules relating to the branching of arteries. One of these states that "all branches which are so small that they scarcely seem to weaken or diminish the main stem come off from it at a large angle, from about 70° to 90°." In general the arteriae nervorum fall into this class and conform to this principle. Occasionally, however, it was noted that a vessel first crossed a nerve before giving off a nutrient branch, which, in order to reach the nerve, traveled in a direction opposite that taken by the parent vessel. Such recurrent branches were given off at an angle exceeding 90 degrees.

Number and Size.—All authors have agreed that the arteriae nervorum are inconstant in both number and size. Bartholdy and Petrovits and Szabo [12] (1939) denied that there is any relation between these two morphologic features, though Ramage [9] stated that when the vessels are smaller they tend to be more numerous. The results of the present investigation suggest that there is a relation between the number and the size of the arteries, and for this reason the two variables will be considered together.

(*a*) The number of nutrient arteries to any particular nerve varies considerably not only from subject to subject but on the two sides of the body. Bartholdy's[2] observation that larger nerves do not necessarily receive more vessels than do smaller nerves was confirmed in my study.

(*b*) Nerves may run considerable distances without receiving a nutrient vessel, the circulation being maintained by large descending intraneural channels. Thus, the median and ulnar nerves were seen free of entering vessels between the axilla and the elbow, nourishment over this length of the nerve being provided by large intraneural channels descending from arteries which had entered the nerve high in the axilla.

(*c*) Despite the variability in the number, site of origin and site of entry into the nerve of the arteriae nervorum, their disposition may be such, particularly in certain regions, that it is impossible to free the nerve from the surrounding tissues for more than a few centimeters without sacrificing some of the vessels supplying it.

(*d*) The caliber of the nutrient arteries fluctuates over wide limits. The largest such artery dissected in the arm measured 1 mm. in diameter, while the smallest could best be described as threadlike and required the aid of dissecting spectacles to trace it to the nerve. Bartholdy [2] stated that a diameter of 1 mm. is rarely exceeded, while the largest artery recorded by Tonkoff [3a] was 0.5 mm. in diameter. Bartholdy [2] denied that larger nerves receive larger arteries than smaller nerves. Though it is true that larger nerves do not necessarily or invariably

11. Roux, W., cited by Thompson, D. W.: On the Form and Branching of Blood Vessels, in Growth and Form, London, Cambridge University Press, 1917.

12. Petrovits, L., and Szabó, Z.: Die arterielle Versorgung der Gliedmassennerven, Anat. Anz. **88**:392, 1939.

receive larger arteries, it was observed that the largest vessels present run to the largest nerves. For example, the arteries from the perforating arteries to the sciatic nerve are conspicuous for their size. Ramage's [9] observation that the largest arteriae nervorum in the upper limb are present in the upper portion was confirmed.

(*e*) Both the size and the number must be taken into consideration when one is estimating the relative vascularity of different segments of the same nerve and of corresponding segments of different nerves. Macroscopic and microscopic investigations suggested that the two are inversely related, but no measurements were taken of the capillary bed to confirm or disprove this assumption. The important function of the arteriae nervorum is the maintenance of the intraneural vascular plexus, and this may be accomplished in a variety of ways. If a large vessel, or vessels, enters the nerve, the plexus will be maintained for a considerable distance before reenforcement becomes necessary. Thus, the median nerve has been seen extending from the axilla to the cubital fossa without receiving a single nutrient artery. Section of such a nerve reveals the presence of large descending intraneural channels derived from a vessel, or vessels, which enter the nerve in the axilla and which are sufficiently large to maintain a functionally effective pattern as far as the elbow. If, however, a small vessel enters the nerve, the process must be repeated at short intervals to achieve the same result. Consequently, under the latter conditions there is a rapid succession of many small vessels entering the nerve, though these need not be evenly spaced or of equal size. The size of the first branches to enter a nerve appears to determine the subsequent size and number of the branches entering it at more distal levels.

(f) The observation of Petrovits and Szabó [12] that the proximal portion of the nerve receives more, larger and longer nutrient arteries has not been confirmed.

(*g*) Most investigators claim that the number of arteries supplying a given length of nerve increases as the nerve passes distally. According to Bartholdy,[2] this is due to the fact that at distal levels the nerve enters regions of greater vascularity. Reference to the tables giving the number of arteries supplying the various nerves along their course shows that such an increase in number at distal levels was unusual in the case of the median nerve and was present in only approximately 50 per cent of the ulnar nerves examined.

Length.—The size and length of the arteriae nervorum were observed to be independent features, though Bartholdy [2] asserted that they were proportional to one another. The length appeared to be determined solely by the proximity of the parent vessel to the nerve—the closer the parent artery the shorter the nutrient branch.

In general, the arteriae nervorum are short, running a course of from ¼ to ½ inch (0.63 to 1.27 cm.) before reaching the nerve, but on occasion, particularly in the supply from the radial artery to the median nerve in the forearm, branches up 1 inch (2.54 cm.) in length are present.

Short, stout nutrient arteries can securely anchor a nerve to a neighboring vascular channel and render its mobilization less easy than one would expect. This, for example, is seen at the medial epicondyle and in the distal half of the forearm, where the ulnar nerve is often securely attached, in the manner described, to the ulnar collateral–posterior ulnar recurrent anastomosis and the ulnar artery respectively.

Course.—The vessels take the most direct route to the nerve and are therefore straight or gently curved; it is unusual to see them running a tortuous course. They establish contact with the nerve on that aspect which is directed toward the accompanying parent vascular channel, and only rarely on the side opposite it. These observations confirm those originally made by Bartholdy.[2]

Occasionally, however, a muscular branch, after having crossed the nerve on its way to its destination, gives off a recurrent nutrient twig, which runs back to enter the nerve on the aspect opposite that at which the direct nutrient arteries were entering. This was seen most commonly in the forearm, particularly toward the wrist, where muscular branches of the radial and ulnar arteries first crossed the median and ulnar nerves before sending a supply back to them.

Behavior of Artery on Reaching the Nerve.—Bartholdy [2] gave a detailed account of the manner in which the arteriae nervorum behave when they approach or establish contact with the nerve they are destined to supply. The results of the present investigation are represented diagrammatically in figure 2, and they are in general agreement with the observations of Bartholdy.

1. The vessel plunges immediately into the nerve without any preliminary extraneural branching. The vessel may enter at a right angle or at an acute or an obtuse angle (i. e., against the direction in which the nerve is traveling). Quénu and Lejars,[1b] on the contrary, stated that an artery never plunges directly into a nerve but always divides before penetrating it, while, in their opinion, nutrient arteries never enter the nerve at right angles.

2. The vessel turns distally on or at a varying distance from the surface of the nerve and forms a superficial descending longitudinal channel of supply which enters the nerve after a varying course or anastomoses on the surface at more distal levels with newly added vessels. Bartholdy [2] did not mention this form.

3. The vessel may descend on the surface of the nerve and then leave, giving off penetrating vessels while accompanying the nerve. Hyrtl's observation [7a] that once an artery joins a nerve it never leaves it has not been confirmed.

of a superficial longitudinal channel, from which the intraneural vessels are in turn derived, or one or both branches may behave in the manner described in section 3. In agreement with the observations of Quénu and Lejars [1b] and Tonkoff,[3a] this T-shaped division is the most common pattern assumed by a nutrient artery when it reaches the nerve.

(*c*) The vessel may divide in spray fashion adjacent to or on the nerve. The radiating branches then adopt one of the patterns already outlined. Such a pattern was recorded by Quénu and Lejars [1b] and by Petrovits and Szabó.[12]

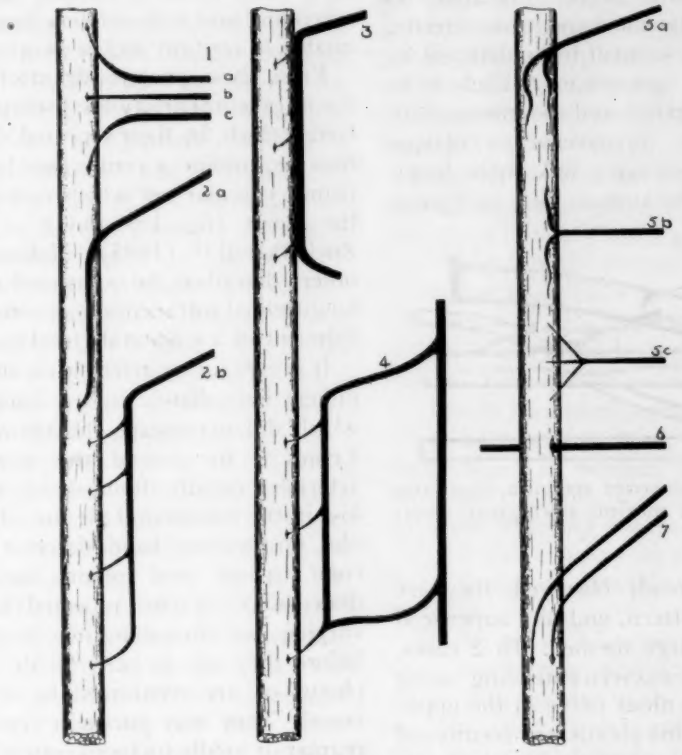

Fig. 2.—Diagram illustrating the manner in which the arteriae nervorum behave as they approach or establish contact with the nerve.

4. The nerve may be supplied from an arterial loop in the manner indicated in figure 2.

5. The nutrient artery divides on or at a varying distance from the nerve. The branches then behave as follows:

(*a*) Both branches descend on the surface, thereby outlining parallel longitudinal channels in the epineurium. It is rare to see both branches ascending on the surface.

(*b*) The branches separate to outline ascending and descending channels, which may be of equal or of unequal size—if they are unequal, the descending channel is usually, but not invariably, the larger of the two. The branches may, in turn, enter the nerve and assist in the formation

Bartholdy [2] referred to this form but stated that he had never seen it.

6. Occasionally an artery may perforate a nerve on its way to supply another structure, but, as Bartholdy has already pointed out, such a perforating vessel may or may not supply the nerve as it passes through it. Such an arrangement is commonly seen in the posterior tibial nerve in the distal third of the leg.

7. Two vessels are occasionally seen to enter a nerve at the same level.

8. When large nerve trunks run in close proximity to each other, notably in the axilla, it is common to see a nutrient artery dividing to

supply two or more nerves (fig. 3). The only other reference to such an arrangement is that made by Tonkoff.[1a]

INTRANEURAL VASCULAR PATTERN

It is common to see, particularly in the upper part of the arm, one or several longitudinally directed macroscopic vessels on the surface of a large peripheral nerve. These vessels, which are arteriolar in type, anastomose with similarly disposed vessels at more distal levels to outline a superficial vascular chain, or chains, of variable length. They run in the epineurium, and from them branches enter the nerve. Precapillaries and capillaries may enter the epineurium directly, but these vessels are too small to be detected by dissection. If present, they are more likely to be restricted to the epineurium and the interfascicular connective tissue. Transverse or oblique anastomoses may occasionally link these longitudinal channels on the surface, but, as Quénu

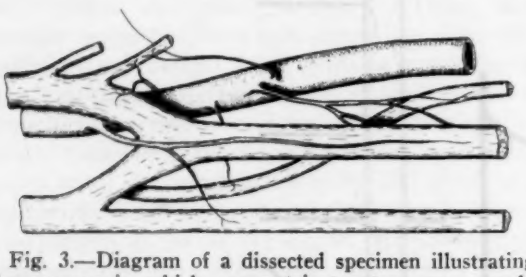

Fig. 3.—Diagram of a dissected specimen illustrating the manner in which one nutrient artery may supply more than one nerve.

and Lejars [1b] have already observed, they are not a feature of the pattern, and any superficial nets so outlined are large meshed. In 2 cases, however, a dense plexus was seen extending along the entire length of the ulnar nerve in the upper arm. In each instance this plexus was reenforced at frequent intervals by numerous small vessels which emerged from the muscles on which the nerve was descending. Such an anastomotic maze has also been seen on the median nerve in the forearm.

A vessel, on entering a nerve, may be distributed in one of several ways. In this investigation the various intraneural patterns of division observed, irrespective of the origin of the vessel, closely resembled the patterns already described for the vessel as it approachced the nerve externally. The fanlike distribution referred to by Bartholdy [2] and by Petrovits and Szabó [12] was seen, but, as Bartholdy admitted, this arrangement is uncommon.

Bartholdy [2] expressed the opinion that if the nutrient artery enters the nerve without any preliminary extraneural branching it divides almost immediately into an ascending and a descending branch, which may be of equal or of unequal caliber; in the latter event the branch which continues in the direction of the parent channel is the larger. If, on the other hand, the nutrient artery has already divided external to the nerve, its penetrating branches undergo no further division into ascending and descending branches within the nerve but turn, following the direction in which they entered, parallel with the longitudinal axis of the nerve. Bartholdy therefore concluded that every nutrient artery, before breaking up into its finer branches, divides at least once, inside or outside the nerve, into an ascending and a descending branch. I have been unable to confirm such a generalization.

From these penetrating arterioles are derived the intraneural arterioles, precapillaries and capillaries which, by their repeated division and anastomosis, outline a continuous longitudinal intraneural vascular net which extends the length of the nerve (fig. 1 *B* and *C*). Holl [13] (1880), Zuckerkandl [14] (1885), Makins [15] (1919) and others described the occasional utilization of this longitudinal intraneural anastomosis in the establishment of a collateral circulation in the limbs.

It is rare for an arteriole on entering a nerve to plunge immediately into a fasciculus—a feature which did not escape the notice of Quénu and Lejars.[1b] In general the smaller penetrating arterioles rapidly diminish in size and are soon lost in the intraneural plexus. The larger arterioles, on the other hand, descend in the interfascicular spaces and retain their identity and dimensions, despite repeated branchings, over varying, but often extensive, lengths of the nerve before they are in turn finally absorbed in the plexus or are reenforced by a newly entering vessel. They may pursue a vertical, oblique, irregular or mildly tortuous course as they descend. The branching of these penetrating arterioles in the interfascicular tissues results in the formation of a series of longitudinally disposed channels, arteriolar or precapillary in type, which are linked at irregular intervals by transverse or oblique anastomoses. These epineurial and interfascicular arterioles and precapillaries represent the largest vessels observed in the nerve and form the basis of the intraneural vascular pattern.

13. Holl, M.: Verrenkung des linken Ellbogengelenkes mit Zerreissung der A. ulnaris und der N. medianus und ulnaris, Med. Jahrb. **10**:151, 1880; cited by Tonkoff.[3]

14. Zuckerkandl, O.: Zwei Fälle von Collateralkreislauf, Med. Jahrb. **15**:273, 1885; cited by Tonkoff [3a]; cited by Poirier, P., and Charpy, A.: Traité d'anatomie humaine, ed. 2, Paris, Masson & Cie, 1909, vol. 3, p. 633.

15. Makins, G. H.: Gunshot Injuries to Blood-Vessels, Bristol, J. Wright & Sons, 1919.

From them, finer branches pass directly into the fasciculi, or to the perineurium, from which they subsequently enter the fasciculi. These branches, which are capillary and precapillary in type, are, in turn, longitudinally disposed in these situations. Capillaries predominate in the fasciculus and precapillaries in the perineurium; the terminal intrafascicular capillary meshwork is established by their repeated branching and anastomoses. Inside the fasciculus the vessels are localized to the intrafascicular connective tissue septums. The statement by Adams [16] that the capillary plexuses alone extend into the endoneurium is incorrect (fig. 4 *C*).

Thus it is customary to find four systems of vessels disposed parallel with the longitudinal axis of the nerve. The vascular systems in the epineurium and in the interfascicular tissues are composed of arterioles and precapillaries, while the vessels in the perineurium and in the fasciculi are composed of capillaries and precapillaries. These longitudinally directed channels repeatedly give off side branches, more or less at right angles, in all directions at frequent, but irregular, intervals. These branchlets, in turn, divide and redivide in a similar manner and finally anastomose to give a terminal vascular net composed of rectangular meshes, which tend to be alined in the longitudinal axis of the nerve.

Serial histologic sections demonstrate that the number, size and position of the longitudinally directed interfascicular vessels vary from one level to another. One or several vessels may be noted in this situation (fig. 4 *A*, *B* and *C*). When several vessels are present, one is usually larger than the others. The relation between size and number observed in the extraneural distribution also obtains for the interfascicular arteriolar pattern. Thus, there may be one large interfascicular arteriole, many small ones or a combination of vessels of varying size.

Observations suggest that the larger the nerve trunk the larger are the arterioles it carries.

No single vessel was observed to dominate the pattern over the entire length of the nerve. In the case both of the median and of the ulnar nerve a large vessel, located on the inner surface of the nerve, has occasionally been observed descending from the axilla to the elbow without interruption and without any alteration of position. This must be regarded as uncommon, for it is more usual for the major intraneural channel of one segment to be replaced as the nerve descends by a newly entering arteriole.

The variation in number of the interfascicular arterioles is due to the repeated division of a large arteriole or to the entrance of new vessels. Both factors influence the number of vessels present at any particular level. However, it was not possible to ascertain with certainty whether the site of redistribution of the nerve fibers and the formation of additional, but smaller, fasciculi are related to the site of entry of new vessels or to the division of vessels already contained with the nerve (fig. 5).

The variation in position is determined not only by the entrance of new vessels but by the alteration in position of interfascicular vessels already descending in the nerve. Such an alteration in position appears to be influenced to some extent by the regrouping of the nerve fibers, which results in a modification of the intraneural fascicular pattern (fig. 5).

There is a general tendency, as Ramage [9] originally pointed out, for the largest vessels to be arranged toward the center of the nerve in the forearm and at the periphery in the upper arm. There are exceptions to such a generalization (fig. 4 *A* and *B*), the most notable being the median artery, which usually descends on the surface of the median nerve in the forearm.

Though the interfascicular arteriolar pattern varies from level to level, from side to side and from subject to subject, the manner of formation and the structure of the terminal intrafascicular capillary meshwork strongly suggest that the blood supply to individual nerve fibers is, on anatomic grounds at least, substantially the same.

As the nerve branches, the vascular net behaves accordingly, and a vascular net commensurate with the size of the branch separates with it. The neural and vascular divisions are often seen for some distance proximal to the point where actual separation takes place. It is to be noted, also, that after the branches of nerves have completely separated from the parent nerve they may receive separate nutrient arteries.

The manner in which the intraneural pattern is maintained and reenforced is of fundamental importance. A characteristic feature is the considerable overlap of supply which obtains between nutrient arteries entering the nerve at different levels. This makes it extremely difficult to determine how much of a nerve is supplied by a single nutrient artery. The arrangement seems to be such that no vessel can be said to supply a precise and discrete segment of a nerve, as some authors have claimed. Petrovits and Szabó [12] alone described the arteriae nervorum as "end arteries." Other authors, however, while admitting the existence

16. Adams, W. E.: The Blood Supply of Nerves: II. The Effects of Exclusion of Its Regional Sources of Supply on the Sciatic Nerve of the Rabbit, J. Anat. 77:243, 1943.

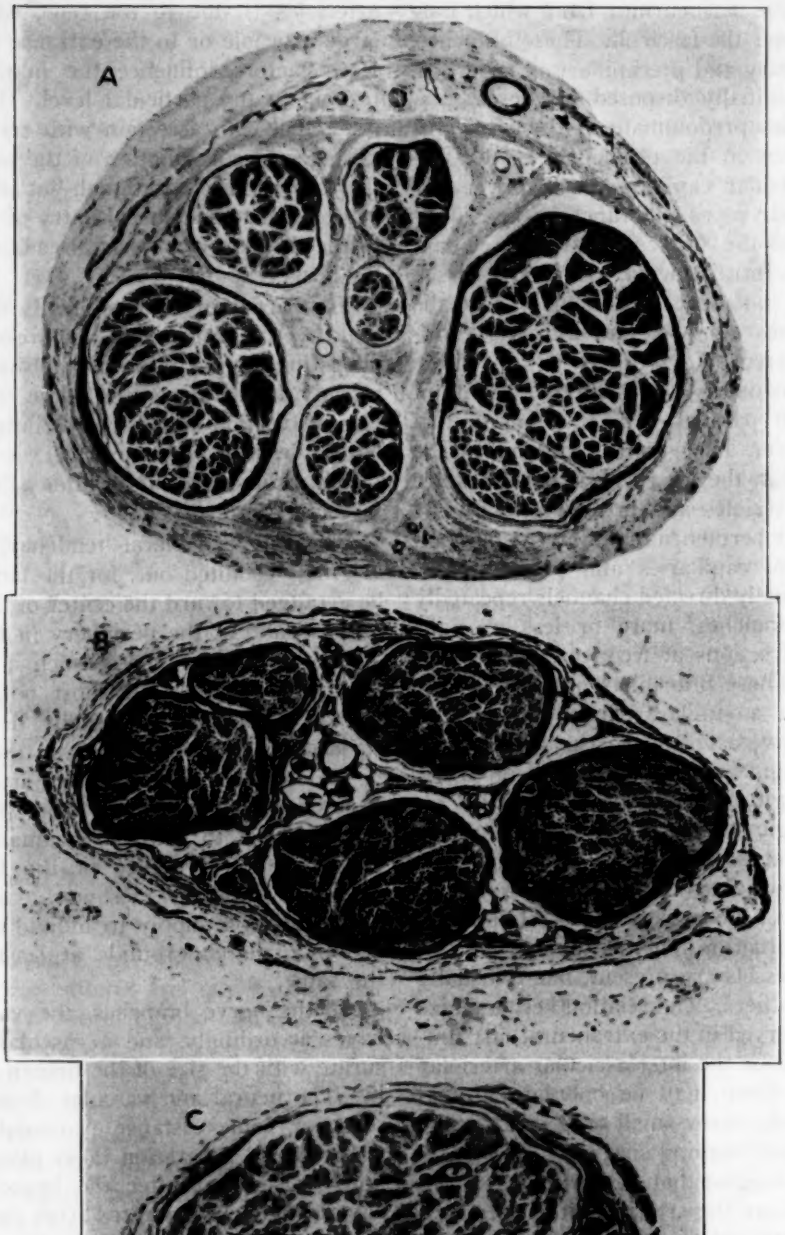

Fig. 4.—*A*, transverse section of the median nerve in the upper arm; × 29. Note the relation of the vessels to the components of the nerve and the presence of a peripherally situated major arteriole. *B*, transverse section of the ulnar nerve in the upper arm; × 38. Note the relation of the vessels to the components of the nerve and the presence of a centrally situated major arteriole. *C*, transverse section of the ulnar nerve in the upper arm; × 27. Note the presence of a large precapillary inside a fasciculus.

of longitudinal anastomosing channels, stated that each nutrient artery dominates the intraneural circulation in its own region. Whether or not this is so remains to be established by experimental investigations into the functional significance of the supply. The physiologic evidence at present available is inconclusive. Adams [16] recently investigated the effects of exclusion of the regional sources of the vascular supply on the sciatic nerve of the rabbit. He

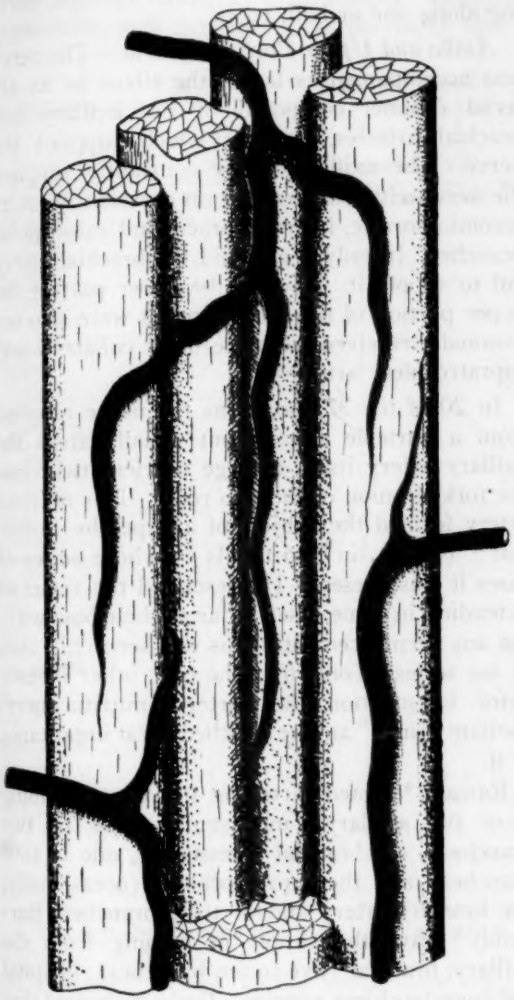

Fig. 5.—Diagram illustrating the manner in which the number, size and position of the intraneural arterioles vary along the course of the nerve.

claimed that such exclusion resulted, in all but 2 cases, either in no or in limited and insignificant degeneration. In the 2 cases extensive degeneration occurred, but Adams was uncertain whether this was to be attributed to manipulation of the nerves or to a variation in their intrinsic vascular pattern. Both the overlap and the profuse and extensive character of the anastomoses render such a conception extremely unlikely. Admittedly, there are instances, though they are uncommon, in which one vessel supplies long stretches of a nerve without reenforcement, but it has been demonstrated in sectioned and injected material that even under such apparently adverse conditions of supply the anastomosis is of such dimensions at the peripheral limits of the solitary channel that segmental ischemia due to the blocking of such a single vessel is a remote possibility. During this study nerves were frequently stripped at operation of all surrounding connections for distances up to 10 cm., yet when the nerve was divided distally, the cut end of the freed segment continued to bleed profusely. The results may be serious, however, if all the vessels to the nerve are affected simultaneously in a generalized sclerosing condition. The establishment of an effective collateral circulation is then no longer possible, and the conducting elements consequently suffer. Again, compression of a length of nerve by a pressure exceeding the arterial pressure prevents blood from entering the compressed segment. Under these conditions, however, it is difficult to determine whether the effects of such an experimental procedure are due to the local ischemia or to the pressure whereby it is produced.

VEINS

Quénu and Lejars [1b] alone carefully examined the venous drainage of the peripheral nerves. They studied in turn, the veins of the cutaneous nerves, the veins of the deep nerves and the veins of the nerve plexuses and recorded the following observations:

1. The main cutaneous nerves almost always accompany a large subcutaneous vein. Nevertheless, the veins of the cutaneous nerves drain predominantly into muscle veins beneath the deep fascia. These authors claimed that any drainage to the subcutaneous venous system is insignificant.

2. The veins of the deep nerves always drain to muscular veins or to the venous plexus in the wall of a neighboring artery. They never drain to the principal vein, or veins, accompanying the artery. Quénu and Lejars claimed to have demonstrated an intimate relation between the veins of the muscles and the veins of the nerves by which the two form a neuromuscular venous system. They attributed a functional significance to this arrangement and claimed that the muscular contractions which aid the venous drainage of the muscles automatically aid the venous drainage of the nerves.

3. The veins draining the nerve plexuses empty into collateral venous channels which have

a muscular origin. It is claimed that the neuromuscular venous relations are the same as venous relations described for the large peripheral nerves in the limbs.

4. The mode of emergence of veins from the nerve and the intraneural venous pattern correspond essentially to the arterial arrangement. The arteries and the veins enter and leave together.

The following additional observations were made in the present investigation:

1. Venules are the largest venous vessels seen in and leaving the nerve.

2. In general, the structure of the intraneural venous pattern corresponds to the arterial arrangement. Venules and arterioles do not always run together, however, either inside or outside the nerve, while counts suggest that the number of interfascicular venules slightly exceeds the number of arterioles.

3. Bichat [6] claimed that in the larger nerves the emerging veins bear a resemblance to the cerebral veins in that they leave the nerve independently of the entering arterioles. This arrangement, though commonly seen, is by no means invariable, for veins and arteries frequently leave and enter the nerve at the same time.

4. The number of venules leaving the nerve does not always correspond with the number of arteries entering the nerve.

5. It is not uncommon to see two veins emerging from the nerve, one on each side of an entering artery.

6. Though the mode of termination of veins from deep nerves, as described by Quénu and Lejars, is common, large emerging veins have been repeatedly seen entering the principal veins.

7. Observations on the venous drainage of the cutaneous nerves have been limited, but they suggest that, though the arrangement described by Quénu and Lejars is the more usual, a drainage into the subcutaneous venous system is not as uncommon as they claimed.

BLOOD SUPPLY OF THE MEDIAN, ULNAR AND RADIAL NERVES

Though the papers of Quénu and Lejars,[1b] Bartholdy,[2] Tonkoff [3] and Bourguet [17] all contain references to the blood supply of individual peripheral nerves, these reports lack the detail provided by Ramage,[9] who confined his investigation to an examination of the blood supply to the large peripheral nerves in the upper limb. The results of the present study will first be described and then compared with the observations previously reported.

MEDIAN NERVE

The source and number of the arteriae nervorum in the dissected specimens are set out in table 1. The supply recorded as coming from the axillary artery includes the vessels which reached the nerve, not directly, but by descending along one or both roots.

Axilla and Upper Portion of Arm.—The nerve was accompanied as far as the elbow by an arterial channel composed of the axillary and brachial arteries, both of which supplied the nerve. The axillary artery constantly supplied the nerve, either directly or on occasion, from its acromiothoracic, lateral thoracic and subscapular branches. In only 1 case did the brachial artery fail to supply it. Toward the lower part of the upper portion of the arm branches were also occasionally received from the ulnar collateral and supratrochlear arteries.

In 20 of the 37 specimens the nerve received from a variable source, but usually from the axillary artery itself, a large nutrient twig into the forked union of the two roots. This nutrient artery formed the subject of a paper by Robinson [18] (1910), in two thirds of whose series of cases it was present. He described the vessel as extending in some cases as far as the elbow without any reenforcement. This was seen only once in my series. Tonkoff is the only other investigator to mention the "arteria nutritia nervi mediani prima," and he attached great importance to it.

Ramage [9] listed arteriae nervorum coming from the axillary (inconstantly, one to two branches), the brachial (constantly, one to four branches) and the supratrochlear (occasionally, one branch) artery and/or their branches. Bartholdy [2] gave the supply as coming from the axillary, brachial (five to ten branches), bicipital and supratrochlear arteries. Tonkoff claimed that the supply is derived from the axillary, brachial (one to four branches), bicipital (frequently one branch) and supratrochlear (one to two branches) arteries. Quénu and Lejars [1] stated that the median nerve receives branches from the brachial and the supratrochlear artery. They gave no details but stated that the supratrochlear almost always sends it a branch. According to Bourguet, the brachial artery gives off only a small number of branches to the nerve in the

17. Bourguet, M.: Des vasa nervorum, Compt. rend. Soc. de biol. **77**:656, 1913.

18. Robinson, R.: Les vaisseaux de la fourche du nerf médian, Compt. rend. Acad. d. sc. **151**:535, 1910.

upper part of the arm, and these branches have long intraneural courses. He expressed the belief that almost the entire brachial portion of the nerve is nourished by a single nutrient artery. In the light of the present observations and results of other investigators, this must be regarded as being unusual.

Cubital Fossa.—In the cubital fossa the nerve was related to the termination of the brachial artery, the first part of the radial and ulnar arteries and the common interosseous, anterior interosseous and anterior ulnar recurrent arteries. Nutrient vessels to the nerve were traced from one or more of these arteries or their branches.

Table 1.—*Arterial Supply of the Median Nerve*

	Axillary		Brachial		Ulnar Collateral	Supratrochlear	Common Anterior Interosseous		Ulnar Recurrent	Median	Radial	Indirect Supply to Forearm, Origin Unknown
	Direct *	Indirect	Direct	Indirect			Ulnar					
1 Left	3	—	1	1	—	—	—	—	1	1	—	—
Right	4	—	7	1	—	1	—	—	—	1	2	1
2 Left	3	—	4	1	—	—	2	—	—	1	4	—
Right	1	—	5	—	—	—	—	—	—	—	1	2
3 Left	3	—	3	—	—	—	1	—	—	1	1	—
Right	1	—	3	—	—	—	5	—	—	—	—	4
	1 A-Th.											
	1 L.Th.											
4 Left	3	—	5	—	—	—	2	—	—	1	—	—
Right	1	1	2	1	—	—	1	—	1	—	1	—
5 Left	2	1	1	1	—	—	—	—	1	—	—	—
Right	1	4	2	1	—	—	—	—	—	1	1	—
6 Left	2	—	6	—	—	—	—	—	—	1	—	—
Right	3	—	2	1	1	1	—	—	1	1	—	—
7 Left	3	—	—	—	—	2	—	—	—	1	—	2
Right	3	—	1	—	—	—	—	—	—	1	1	—
8 Left	1	—	3	—	—	—	—	—	—	1	—	4
Right	2	—	2	1	—	—	—	—	—	—	3	2
9	1	—	1	2	3	—	1	3	—	1	3	3
10	3	—	2	—	—	—	1	—	1	—	—	2
11	3	—	4	—	—	1	2	—	—	1	1	2
12	1	—	5	—	—	—	1	—	—	1	—	—
	1 A-Th.											
13	2	—	7	1	—	—	—	—	—	1	1	—
	1 L.Th.											
14	2	1	4	—	—	—	—	—	—	1	—	—
15	1	—	4	—	—	—	—	—	—	1	—	—
16	2	—	5	1	—	—	—	—	—	1	—	1
17	3	—	3	1	—	—	—	—	—	1	2	1
18	1	—	5	1	—	2	—	—	—	—	—	2
19	—	1	3	4	—	—	1	—	—	—	—	—
20	5	—	8	—	—	—	—	—	—	1	4	—
	1 Subs.											
21	—	1	5	—	—	—	—	—	—	1	1	—
22	1	—	4	—	—	—	—	2	—	—	1	—
23	1	—	6	1	—	—	—	—	—	1	2	—
	1 Subs.											
24	3	—	2	—	—	1	—	—	—	1	1	—
25	2	—	1	—	2	—	3	—	—	—	—	—
26	1	—	4	—	—	—	—	—	—	1	1	—
27	3	1	3	—	—	—	1	—	—	1	1	—
28	2	1	5	1	—	—	—	—	2	1	1	—
29	2	1	10	—	—	—	—	—	—	1	1	—

* A-Th. indicates the acromiothoracic; L.Th., the lateral thoracic, and Subs., the subscapular artery.

Forearm.—No artery constantly supplied the nerve in the forearm. Vessels were traced to the nerve from the ulnar, radial, common interosseous, anterior interosseous and median arteries, and occasionally also from their muscular branches.

In the forearm the median nerve descends with the radial and ulnar arteries well to its lateral and medial sides respectively and with the anterior interosseous artery on a deeper plane. Thus the vascular relations are not so intimate as in the upper arm, but this lack of a suitably placed major limb artery is frequently compensated for by the presence of the median artery, which accompanies the nerve down the foreram. This investigation confirmed Tonkoff's observation that the nutrient arteries in the forearm vary in number with the development of the median artery, which supplies the nerve exclusively if it is strongly developed. This vessel, which was present in 27 specimens, may take origin from the ulnar, the common interosseous, the anterior ulnar recurrent or the anterior interosseous artery or one of their large muscular branches. In this series it conformed to one of two basic types. In the majority of cases (17 out of 27) it terminated by entering the nerve after pursuing a course of variable length on or near its surface. In the remaining cases the vessel did not enter the nerve but ran on or adjacent to it before finally entering the hand or the flexor muscles on the distal part of the forearm. As the median artery descended on or near the nerve, it gave one or more branchlets to the nerve before finally penetrating or leaving it. Ramage stated the opinion that each branch of the median

artery to the nerve is a separate nutrient vessel. It is preferable, however, and more in keeping with the basic nature of the supply, to regard this vessel and any branches it may give to the nerve externally as a single nutrient system. Arrangements such as have been described for this channel are frequently present elsewhere in the limb and have already been described as types 2 and 3 in the previous section, which deals with the behavior of the nutrient vessel on its approaching the nerve (fig. 2). Since in these positions the nutrient artery and its branches have been considered as a single channel, there can be no justification for departure from this practice in the case of the median artery.

In 3 of 10 specimens in which the median artery was absent the nerve received its last nutrient artery in the cubital fossa.

At the wrist, the radial and ulnar arteries come slightly closer to the nerve as the forearm narrows, and this is the region where these vessels or their branches most commonly supply the median nerve.

Ramage listed arteriae nervorum coming inconstantly from the radial (one to four branches), ulnar (one to four branches), anterior ulnar recurrent (one to two branches), anterior interosseous (one to three branches) and median arteries, and in 1 specimen the nerve received a single branch from the superficial volar artery. Bartholdy gave the supply as coming from the radial and ulnar arteries, from the anastomoses of these two arteries and from the anterior ulnar recurrent, anterior interosseous and median arteries. According to Tonkoff, the supply in the forearm is derived from the "cubital," ulnar, anterior ulnar recurrent and median arteries, from the muscular branches of the anterior interosseous and radial arteries and from the anastomoses between the radial and the ulnar artery. Quénu and Lejars [1] described branches coming from the anterior ulnar recurrent, radial and median arteries. Bourguet stated that the ulnar artery sends a special branch to accompany the nerve, from which a series of arteriae nervorum arise, each of which has a limited area of distribution in the nerve. Such a localized distribution has not been confirmed.

Comment. — There is, among investigators who have submitted the arterial supply to a detailed examination, general agreement concerning the vessels from which the arteriae nervorum are derived. All are of the opinion that the supply from the brachial artery predominates in the upper arm. This is only to be expected when one considers that the vessel accompanies the nerve throughout its course in this region.

In general the number of nutrient arteries recorded in this investigation as reaching the nerve in the upper portion of the arm exceeds the number given by either Ramage or Tonkoff. The figures correspond with those reported by Bartholdy. Though large nutrient arteries are seen in the forearm, the largest observed, with the exception of the median artery, usually occur in the upper arm.

Ramage's observation that the number passing to the nerve in the forearm exceeds the number reaching it in the upper arm has not been confirmed. The variable size of the median artery and the irregular manner in which it supplies the nerve and terminates in relation to it, however, render difficult any comparison between the number of vessels received in the upper arm and that received in the forearm. For reasons already set out, it is proposed, unlike Ramage, to regard the median artery and its arteriae nervorum as a single nutrient system. In this investigation it has been determined that even if the branches of this artery to the nerve are regarded as separate nutrient vessels, the number received by the nerve in the upper arm would, in the majority of cases, still exceed the number received in the forearm. There seems no doubt that the smaller number of nutrient arteries received in the forearm is due to the absence of large neighboring channels of supply. As has already been pointed out, this is compensated for by large descending intraneural vessels or by the addition of a specific nutrient vessel, the median artery, which in the majority of cases in which it is present ends within the nerve. It is to be stressed, however, that the number of vessels passing to a nerve is, in the absence of additional data, of little significance in estimating the blood supply of that nerve, and studies devoted to this feature alone are likely to be misleading.

It is interesting to note the higher incidence of the median artery in fetal, as opposed to adult, material in Ramage's series.

ULNAR NERVE

The ulnar nerve is accompanied throughout its course by a continuous arterial chain derived, in turn, from the axillary, brachial, ulnar collateral, supratrochlear, posterior ulnar recurrent and ulnar arteries. It is from this arterial system that the blood supply of the ulnar nerve is derived. The source and number of the arteriae nervorum are set out in table 2. In this table the supply recorded as coming from the axillary artery includes the vessels which passed

to the medial cord of the plexus and which could be traced distally into the ulnar nerve. Though it is possible to predict with some degree of certainty from which vessels the supply will be derived, it is not possible to foretell, as is clearly brought out in table 2, how many arteriae nervorum the nerve will receive, the numerical contribution of each individual vessel in the system or at what point they will branch from the parent vessel.

Axilla and Upper Portion of Arm.— In this region the axillary artery or its branches constantly supplied the nerve, as did the ulnar collateral artery in every case. According to Bartholdy the nerve is supplied from the axillary artery, the brachial artery and its muscular branches and the ulnar collateral artery. The latter stated that as long as the nerve is near the brachial artery it is supplied from its muscular branches, and only rarely directly from the artery itself, but this is an observation that has not been confirmed by any other investigator. On the other hand, his observation that there are long stretches of the nerve in the upper arm which do not receive any arteries has been confirmed. Ramage in 25 specimens listed the nerve as being supplied by the

TABLE 2.—*Arterial Supply of the Ulnar Nerve*

	Axillary		Brachial		Profunda	Radial	Ulnar Collateral		Supratrochlear	Posterior Ulnar Recurrent		Ulnar	
	Direct*	Indirect	Direct	Indirect			Direct	Indirect		Direct	Indirect	Direct	Indirect
1 Left	3	—	1	—	—	—	—	—	1	2	—	10	—
Right	4	—	1	—	—	—	2	6	—	2	—	8	1
2 Left	2	—	—	1	—	—	7	—	—	4	—	15	—
Right	1	—	1	—	—	—	4	—	—	2	—	15	—
3 Left	1 Subs.	—	—	—	—	—	2	—	1	2	—	6	—
Right	3	—	—	—	—	—	4	—	—	2	—	3	—
4 Left	2	—	1	—	—	—	2	—	2	3	—	4	2
Right	1 Ach	—	—	—	—	—	4	—	—	2	—	5	—
5 Left	1	—	2	—	—	—	1	—	2	1	—	4	—
Right	1	2	1	—	—	—	3	1	—	3	—	5	1
6 Left	3	—	2	—	—	—	1	—	1	3	—	6	—
Right	3	—	—	1	—	—	5	—	—	3	—	5	—
7 Left	1	—	—	—	—	—	2	—	—	2	—	2	—
Right	2	—	—	—	—	—	4	—	—	2	—	4	—
8 Left	1	1	1	—	—	—	4	—	—	2	—	5	—
Right	1	—	—	—	—	—	3	—	—	1	—	7	—
9	2	—	—	—	—	—	1	—	—	3	—	6	—
10	1	—	—	—	—	—	2	5	—	2	—	8	—
11	2	—	—	—	—	—	5	—	—	4	—	8	—
12	1	—	1	1	—	—	3	—	—	2	—	8	—
13	2	—	2	2	—	—	4	—	—	2	1	6	—
14	1	—	3	—	—	—	2	—	2	1	—	6	—
15	1	—	—	—	—	—	3	—	—	1	—	8	—
16	1	—	—	—	—	3	5	—	—	4	—	12	—
17	—	1	—	—	—	—	3	—	—	1	—	4	—
18	1 Subs.	—	—	—	2	—	1	—	1	1	—	4	—
19	2	—	—	2	—	—	1	—	1	2	—	1	—
20	3	1	—	—	—	—	2	—	—	1	—	6	—
21	2	—	—	—	—	—	4	1	—	1	—	1	—
22	1 Subs.	—	—	—	—	—	4	—	2	2	—	4	—
23	1	—	—	—	—	—	5	—	1	1	—	5	—
24	2	1	—	—	—	—	2	—	5	2	—	7	—
25	2	—	—	—	3	—	2	—	4	2	—	1	—
26	1	—	—	—	—	—	4	—	2	1	—	4	—
27	3	—	1	—	—	—	2	—	1	1	—	1	—
28	—	1	—	—	—	—	4	—	1	1	—	3	—
29	1	—	1	—	—	—	6	—	2	2	—	2	—

* Ach indicates the anterior circumflex humeral, and Subs., the subscapular artery.

lateral artery in every specimen but one, while the brachial and supratrochlear arteries supplied it only irregularly. In the majority of specimens the main source of supply was from the ulnar collateral artery. When nutrient branches from this vessel were absent or few the nerve was nourished by large channels descending intraneurally from the axilla. Occasionally the arteria profunda brachii and a high radial artery obtained a sufficiently intimate relation to the nerve to supply it.

Tonkoff described arteriae nervorum from the axillary and ulnar collateral (one to four branches) arteries, with an occasional one from a muscular branch of the brachial artery. He attributed the main supply to the ulnar collateral ulnar collateral artery (one to four branches) in every specimen and by the axillary artery in all but 2 specimens (one direct branch from the main trunk in 21 specimens and one branch from the subscapular artery in 2 specimens); a supply was also derived inconstantly from the supratrochlear artery (one to two branches) and very occasionally from the brachial (one branch in 5 specimens and two branches in 1 specimen) and the profunda (one branch in 3 specimens) artery.

Region of the Medial Epicondyle.—Attention is drawn to the constant blood supply received by the nerve in the vicinity of the medial epicondyle. The ulnar collateral, supratrochlear and posterior ulnar recurrent arteries participate in the formation of an anastomotic system which is closely

associated with the nerve as the latter curves around the medial epicondyle. The nerve may be firmly anchored in this position by short nutrient arteries passing directly to it from the anastomotic channel, and these vessels must be sacrificed to permit adequate mobilization of the nerve when it is being transplanted anterior to the epicondyle. This anastomosis is often of such dimensions that it is difficult to determine where one vessel ends and another begins. Consequently it is difficult at times to ascertain from which particular artery a nutrient vessel is taking origin. The figures given are as accurate as the investigation permitted.

Tonkoff described one to three branches entering the nerve from this anastomosis. Bartholdy noted in his series that the vessels to the nerve were exceedingly well injected in this region, though in his account he mentioned only a supply from the posterior ulnar recurrent artery and from a muscular branch to the flexor carpi ulnaris muscle.

Forearm.—From the medial epicondyle to the wrist the nerve is accompanied in turn by the posterior ulnar recurrent and the ulnar artery, and these vessels, particularly the ulnar, send many nutrient arteries to the nerve. The ulnar artery is usually closely applied to the nerve in the distal one half to two thirds of the forearm, and the arteriae nervorum are consequently short and pass directly into the nerve.

Tonkoff described a branch from the posterior ulnar recurrent artery or its muscular branches in the upper third of the forearm and two or three branches from the ulnar artery or its muscular branches in the distal two thirds of the forearm. According to Ramage, the nerve in the forearm is supplied constantly from the posterior ulnar recurrent (one to three branches) and the ulnar (one to seven branches) artery. He gave a higher incidence of indirect nutrient branches from the latter than was recorded in the present investigation. Bartholdy claimed that the nerve is always supplied by the ulnar artery at 2 cm. intervals. This regularity was seen on occasions, but it was certainly not a feature of the supply.

Comment.—There is general agreement concerning the vessels from which the arteriae nervorum take origin. All investigators are of the opinion that in the upper arm the nerve is supplied principally by the ulnar collateral artery and that in the forearm a large number of arteriae nervorum are received from the posterior ulnar recurrent and ulnar arteries. In general the number recorded in the present investigation as reaching the nerve in the upper arm exceeded that given by Ramage and by Tonkoff. The number of indirect arteriae nervorum observed in the forearm was less than that reported by Ramage.

As in the case of the median nerve, the figures presented by Ramage indicate that the number of nutrient arteries passing to the ulnar nerve in the forearm invariably exceeds that reaching it in the upper arm. The present investigation showed, however, that the number of nutrient arteries to the nerve in the forearm as compared with the number to the nerve in the upper arm was as follows:

No. of Nutrient Arteries	No. of Specimens
Equal	3
Greater in the forearm	18
Greater in the upper arm	16

The number received, however, was subject to such extreme ranges of variation that it is believed that any generalization on the data available would be misleading.

RADIAL NERVE

The radial nerve is supplied by the axillary, brachial and profunda brachii arteries and their branches as far as its entry into the spiral groove, by the profunda brachii artery while running in the groove, and, finally, by the anastomosis between the profunda brachii and the anterior radial recurrent artery. This anastomosis is closely related to the nerve as it descends in the intermuscular furrow between the brachialis muscle, medially, and the muscles arising from the supracondylar line, laterally. The source and number of the nutrient arteries in the various regions are set out in table 3.

Ramage, in his account, provided no information concerning the site where the arteriae nervorum take origin from the profunda artery. For this reason, it is convenient to refer to his observations here rather than in the sections relating to the regional supply. In a study of 25 specimens he listed the nerve as being supplied by the following arteries: axillary (one branch, in 7 specimens); subscapular (one to two branches, in 12 specimens); brachial (one to two branches, in 16 specimens); profunda (two to nine branches, in 25 specimens), and anterior radial recurrent (one to three branches, in 14 specimens. Thus the profunda artery alone constantly supplied the nerve and also provided the largest number of nutrient arteries. According to Ramage, the arteriae nervorum from the brachial artery were predominantly indirect and took origin from muscular branches.

Axilla; Arm.—Information concerning the number of arteriae nervorum received from the

axillary, subscapular, brachial and profunda brachii arteries is provided in table 3. The supply recorded as coming from the axillary artery includes the vessels which entered the posterior portion of the cord and which could be traced distally into the radial nerve.

In this region Tonkoff described a constant supply from the subscapular artery, in addition to arteriae nervorum from the profunda artery and/or its muscular branches. He did not mention either the axillary or the brachial artery. Ac-

TABLE 3.—*Arterial Supply of the Radial Nerve**

	Axillary		Brachial, Direct	Profunda			Anterior Radial Recurrent	
	Direct	Indirect		Arm	Groove	Furrow	Direct	Indirect
1 Left	2	—	—	—	2	—	—	2
Right	4	—	1	—	5	—	1	2
2 Left	1 *	—	2	—	4	2	1	—
Right	1	—	1	—	2	1 Ind.	2	—
3 Left	1	—	—	1	1	2	1	—
Right	2	—	—	—	6	3	1	2
4 Left	2	—	—	—	3	—	1	1
Right	1	—	—	—	4	—	2	—
5 Left	1 *	1	—	—	3	1	2	1
Right	3 *	—	—	—	4	—	1	—
6 Left	3	—	—	—	4	2	2	—
Right	1 *	—	—	—	3	—	2	—
7 Left	2	—	—	—	5	—	1	—
Right	2	1	—	—	4	1	1	—
8 Left	2	—	—	—	3	1	1	—
Right	1	—	—	1	2	1	—	—
9	1	—	—	1	3	2	—	1
10	2	—	—	—	3	1 Ind.	1	—
11	1	—	—	—	2	—	2	—
12	2 *	—	—	1	1	2	—	—
13	1	—	1	—	1	2	2	—
14	1							
	1 *	1	—	—	4	2	1	—
15	1 *	—	—	1	2	—	1	1
16	2	—	—	—	9	—	—	—
17	1	—	—	—	1	2	1	—
18	1 *	—	—	1	2	1	—	—
19	1	—	—	1	1	1	1	—
20	1 *	—	—	1	1	1	—	—
21	2	—	—	—	3	1	—	—
22	1 *	—	—	—	3	1	1	—
23	1 *	—	—	—	1	1	2	—
24	2	—	—	1	3	1	1	—
25	1	—	1	1	4	3	—	—
26	1							
	1 *	1	—	1	1	2	1	—
27	2							
	2 *	—	—	—	1	1	—	—
28	1 *	—	1	—	2	1	1	—
29	1	1	2	—	3	3	—	—

* Indicates subscapular artery, and Ind., here and in table 4, indirect blood supply.

cording to Bartholdy the arteriae nervorum are derived from the axillary, profunda and brachial arteries. He stressed the predominance of the supply from the muscular branches of the brachial artery, with which Ramage expressed agreement, but this observation is contrary to the results of the present investigation.

Spiral Groove.—The profunda artery constantly supplied the nerve in this situation. Tonkoff, Bartholdy, Bourguet and Ramage referred to the blood supply from the profunda artery in this region, but Tonkoff (describing two to three branches) and Ramage (describing two to nine branches) alone gave details.

Certain features of the neurovascular arrangements in this region are worthy of comment. Ramage previously commented on the division of the profunda artery, in the majority of cases, into two vessels of almost equal size, called proximal and distal, which accompany the nerve on opposite sides as far as the lateral intermuscular septum. It is the proximal branch which accompanies the nerve through the lateral intermuscular septum. The presence of such an arrangement has been confirmed in this investigation. Ramage distinguished between the nutrient arteries arising from the proximal and those arising from the distal division, but no such distinction was drawn in this study. Again, it is common for many of the branches of the nerve to separate from the main trunk high in the groove but to accompany it for some distance before finally leaving to pass to their destination. Consequently, the radial nerve frequently has the appearance of a collection of loosely arranged strands or collaterals as it descends in the groove. The vascular pattern is modified accordingly. The nerve shows many superimposed vessels; one series is arranged along the principal trunk, while the other is disposed on each of its collateral branches. Bourguet reported a similar arrangement and is the only other investigator to do so. In the present series the number of nutrient branches given in the tables refers only to vessels passing to the principal trunk of the nerve.

Intermuscular Furrow.—In this region the nerve receives its supply by direct, and occasionally by indirect, nutrient arteries from the anastomosis between the profunda and the anterior radial recurrent artery.

Tonkoff mentioned only the source and gave no details. It is often difficult to establish the origin of some of the muscular branches in this region, but it is probable that some of them are originally derived, as Tonkoff stated, from the brachial artery. Bartholdy referred only to the supply from the profunda artery in this region.

Comment.—There is general unanimity concerning the vessels from which the nutrient arteries take origin, and all authors are agreed on the importance of the supply from the subscapular and profunda arteries. The large and constant supply in the spiral groove is a striking feature. In general the number of vessels observed in the present study exceeded the number reported by Ramage and Tonkoff.

Bartholdy claimed that the length of the nerve from its origin to the site of entrance of the first nutrient artery is often 8 to 10 cm. This obser-

vation was confirmed in the present study. Between its origin and its entrance to the spiral groove the nerve received fewer arteries than elsewhere along its course, and frequently this segment of the nerve was supplied solely by descending intraneural channels which reached it from the posterior portion of the cord.

As in the case of the median and ulnar nerves, the direct type of nutrient artery predominates. However, both Bartholdy and Ramage described a larger number of indirect nutrient arteries from the brachial artery than was observed in the present investigation.

As far as the spiral groove the fasciculi of the nerve are compactly arranged, and over this section the largest intraneural arterioles run on or just beneath the surface of the nerve; distal to this point, where the fasciculi are more loosely arranged, the arterioles are scattered irregularly among them.

SUPERFICIAL RADIAL NERVE

The blood supply of this nerve was examined from its origin to the point where it passes on to the dorsum of the forearm. The source and number of vessels reaching it are set out in table 4.

Bartholdy described a supply from the anterior radial recurrent artery and from the muscular and cutaneous branches of the radial artery. Tonkoff referred only to the radial supply, which is represented by four to five twigs from its muscular and cutaneous branches. According to him the nerve is rarely supplied directly from the main artery. Ramage listed a supply from the anterior radial recurrent artery (one to four branches) and from the radial artery (one to four direct and one to five indirect branches). The results of the present investigation were in general agreement with the observations of Ramage.

POSTERIOR INTEROSSEOUS NERVE

The nerve is accompanied by and supplied from the anterior radial recurrent and posterior interosseous arteries, the anastomosis between them in the supinator muscle and occasionally, in the distal part of the forearm, the termination of the anterior interosseous artery after that vessel has pierced the interosseous membrane. The source and number of arteriae nervorum are set out in table 4, and the figures are in general agreement with those given by Ramage. Both Bartholdy and Ramage described a supply from the vessels named, except for the anterior interosseous artery, but Ramage alone provided details of that supply.

TABLE 4.—*Blood Supply of the Superficial Radial and Posterior Interosseus Nerves*

	Superficial Radial Nerve				Posterior Interosseous Nerve					
	Anterior Radial Recurrent		Radial		Anterior Radial Recurrent		Anastomosis, Direct	Posterior Interosseous		Anterior Interosseous
	Direct	Indirect	Direct	Indirect	Direct	Indirect		Direct	Indirect	
1 Left	—	1	2	3	—	—	—	3	—	1
Right	1	—	1	3	—	2	—	1	2	—
2 Left	—	—	2	1	1	—	—	2	—	—
Right	2	—	2	1	—	—	1	—	1	1
3 Left	2	—	1	1	1	—	—	1	—	—
Right	3	—	1	—	1	—	—	2	—	—
4 Left	2	—	3	1	—	—	1 Ind.	—	1	1
Right	—	—	4	—	1	—	—	—	1	—
5 Left	—	—	4	2	—	1	—	1	2	1
Right	1	—	1	3	1	—	—	2	1	—
6 Left	—	—	1	1	1	—	—	2	—	1
Right	—	—	1	2	1	—	—	3	1	—
7 Left	1	—	—	2	—	—	1	1	1	—
Right	1	—	2	2	1	—	1	2	—	—
8 Left	—	—	—	1	1	—	—	2	—	—
Right	—	—	—	—	1	—	—	1	—	1
9	—	—	2	2	2	—	—	—	—	1
10	1	—	—	1	—	—	1	—	—	—
11	—	—	—	—	—	—	1	—	—	1
12	1	—	—	—	—	—	—	2	1	—
13	—	—	2	2	1	—	—	2	1	2
14	1	—	—	1	—	—	2	—	—	1
15	—	—	1	4	2	—	—	—	2	—
16	—	—	—	—	—	—	—	1	1	—
17	—	1	—	2	1	—	—	1	—	—
18	2	—	1	2	—	—	—	3	—	—
19	—	—	3	1	—	—	—	2	—	—
20	1	—	1	—	1	—	—	3	—	2
21	—	—	1	—	—	—	—	3	—	—
22	1	—	—	1	1	1	—	1	1	—
23	—	—	—	2	3	—	—	2	—	1
24	—	—	2	4	3	—	—	1	—	—
25	2	—	1	1	3	—	—	2	—	—
26	1	—	—	2	—	—	—	1	1	1
27	1	—	—	1	1	—	—	3	—	1
28	1	—	—	4	—	1	—	2	—	1
29	1	—	1	2	1	—	—	1	—	2

COMPARISON OF BLOOD SUPPLIES OF MEDIAN, ULNAR AND RADIAL NERVES

An important point to be decided is whether or not there is any significant difference in the blood supply not only of different nerves but of different segments of the same nerve. Before embarking on an investigation to settle this point, one must define exactly what is meant by the blood supply of a nerve. This has not been attempted, so far as I am aware, by any previous investigator. Many workers appear to have regarded the blood supply of a nerve as synonymous with the number of nutrient arteries it receives, but a study of the number of vessels alone can give no true conception of the blood supply of a nerve. Again, one frequently meets with such terms as "blood supply," "richness of blood supply," "richness of vascularization," "greater, better or richer blood supply" and "poorer blood supply," without any qualification to indicate whether the expression refers to the number, size and intraneural distribution of the arteriae nervorum or to the amount of blood reaching the part. "Blood supply" has an anatomic and the other terms a physiologic significance, and they differ in that, though the anatomic arrangement influences the amount of blood reaching the nerve, additional, and highly relevant, factors participate in controlling the supply. Consequently, anatomic studies alone, such as have been undertaken in this investigation, cannot furnish conclusive evidence concerning the actual amount of blood reaching the nerve, though they do provide an essential basis for studies of the latter. It is proposed in this paper to distinguish between the term "blood supply," which will be taken to have a purely anatomic basis, and such terms as "richness of supply," "richness of vascularization" and "better" or "poorer blood supply," which will be taken to have a physiologic implication. It is obvious, then, that on the basis of the observations recorded in this investigation one is justified in comparing, for the three nerves, only the anatomic, and not the physiologic, factors.

Even when employed in a strict anatomic sense, the term "blood supply" requires further elaboration, since it could refer, in turn, to the number or size of the arteriae nervorum, to the structural features of the intraneural pattern, to the supply to the entire nerve trunk, which incidentally involves more tissues than nerve fibers, or to the supply to individual nerve fibers contained in the trunk. For example, the sciatic nerve receives larger and more nutrient arteries than does the axillary nerve. From a consideration of this feature alone it might reasonably be concluded that the sciatic nerve receives a greater blood supply than the axillary nerve, though examination of the intraneural pattern and an analysis of the supply to individual nerve fibers would not necessarily lead to the same conclusion. It has been established that, for all the peripheral nerves examined, the supply to each nerve fiber, irrespective of the peripheral nerve which carries it or of its position in the nerve, is substantially the same. Consequently, in the present discussion the term "blood supply" will be restricted to the supply to the peripheral nerve trunk, and comparison of the supplies to the three nerves has been based on the size and number of the arteriae nervorum received by each nerve and the structure of the intraneural pattern.

It is now proposed to analyze, in the manner outlined, the supply in the 37 specimens examined, in an attempt to detect any significant differences in the blood supply of (1) the median, radial and ulnar nerves in the upper arm, (2) the median nerve in the arm and forearm, (3) the ulnar nerve in the arm and forearm, (4) the median and ulnar nerves in the forearm and (5) the superficial radial and posterior interosseous nerves.

Ramage [9] is, so far as I can ascertain, the only other investigator who has devoted any attention to this problem, but his observations were limited and the methods by which he arrived at his conclusions not always clearly stated. His paper, however, must be reviewed in some detail at this point, since his are the only data available for comparison with the observations made during this investigation.

Ramage examined by the injection method the blood supply of the median, ulnar and radial nerves in 8 adult and 17 fetal arms. His procedure was to dissect and count, in each specimen, the vessels passing to each nerve in the upper arm and the forearm. From the data obtained he averaged the number of nutrient arteries to each individual nerve in both situations. He reported the numbers in the accompanying tabulation as the average per specimen,

	Nutrient Arteries	
Nerve	Arm	Forearm
Median	3.8	6.4
Ulnar	3.8	7.16
Radial	6.2	...

and from these figures he drew his conclusions.

1. The number of arteries passing to a nerve in the forearm exceeds that reaching the nerve in the upper arm. He stated, however, that the branches

are smaller in the forearm and asserted, without producing any further evidence, that "the blood supply is actually better in the upper arm than in the forearm."

2. The number of arteries to the musculospiral nerve exceeds the number to either the median or the ulnar nerve in the upper arm. He admitted that it is difficult to say on the basis of dissections whether or not the blood supply is greater but claimed that a microscopic examination of injected material indicated that it is so. Reference to his observations on the relative vascularity of the superficial radial and posterior interosseous nerves will be made in the section of the text devoted to this question.

Thus Ramage, in establishing his conclusions, worked solely on the basis of the average number of nutrient vessels received per nerve for the whole series. No attempt was made to compare, in each separate specimen, the number passing to each of the three nerves in the upper arm and in the forearm respectively. Such a procedure, and this is the one which has been adopted in this investigation, would have necessitated some modification of his conclusions.

Median, Ulnar and Radial Nerves in the Upper Arm.—The great irregularity in the number of arteriae nervorum is shown in table 5. The ranges of variation are similar for all three nerves, and this makes comparison of them extremely difficult. If, however, the numbers to the three nerves in the same specimen are compared, the following data are obtained:

No. of Nutrient Arteries	No. of Specimens
Radial and Ulnar Nerves	
Equal	9
Greater to the radial	16
Greater to the ulnar	12
Radial and Median Nerves	
Equal	5
Greater to the radial	19
Greater to the median	13
Ulnar and Median Nerves	
Equal	6
Greater to the ulnar	14
Greater to the median	17

Such an analysis admittedly neglects degrees of difference, but it appears to justify the following conclusions:

1. No nerve consistently receives more nutrient arteries than any other.

2. In only a small proportion of cases do nerves receive an equal number of nutrient arteries.

3. Any nerve may receive more nutrient arteries than its fellows.

4. In a small majority of the specimens the number of nutrient arteries to the radial nerve exceeds the number to the ulnar or median nerve, and the number to the median nerve exceeds that to the ulnar nerve. The number of specimens examined is too small, however, to give data of statistical value.

5. On the basis of numbers alone it is impossible to assign a constantly greater blood supply to any one nerve.

TABLE 5.—*Number of Nutrient Arteries Passing to Median, Ulnar, Radial, Superficial Radial and Posterior Interosseous Nerves*

	Median		Ulnar				
	Upper Part of Arm	Forearm	Upper Part of Arm	Forearm	Radial	Superior Radial	Posterior Interosseous
1 Left	5	2	5	12	6	6	4
Right	13	4	13	11	13	5	5
2 Left	8	7	10	10	3	3	3
Right	6	3	6	17	7	5	3
3 Left	6	3	4	8	6	4	2
Right	6	9	7	5	14	4	3
4 Left	8	3	7	9	7	6	3
Right	5	3	5	7	7	4	2
5 Left	5	1	6	5	9	6	5
Right	8	2	8	9	8	5	4
6 Left	8	1	7	9	11	2	4
Right	8	2	9	8	6	3	5
7 Left	5	3	3	4	8	3	3
Right	4	2	6	6	9	5	4
8 Left	4	5	7	7	7	1	3
Right	5	5	4	8	5	—	3
9	7	11	3	9	8	4	3
10	5	4	8	10	7	2	1
11	8	6	7	12	5	—	2
12	7	2	6	10	6	1	3
13	11	2	10	9	7	4	6
14	7	1	8	7	10	2	3
15	5	1	4	9	6	5	4
16	8	2	9	16	11	—	2
17	7	4	4	5	5	3	2
18	9	2	5	5	5	5	3
19	8	1	6	3	5	4	2
20	14	5	6	7	4	2	6
21	6	2	7	2	6	1	3
22	5	3	7	6	6	2	4
23	9	3	7	6	5	2	6
24	6	2	10	9	8	6	4
25	5	3	11	3	10	4	5
26	5	2	7	5	8	3	3
27	7	3	7	2	6	2	3
28	9	4	6	4	6	5	4
29	13	2	10	4	10	4	4

The size of the arteriae nervorum is subject to substantially the same variations in each nerve in the same specimen. Thus, the largest vessel to one nerve can be matched in size by an arteriole to another nerve. In this connection, however, the relation between size and number should not be neglected. From the study of size alone it is impossible to assign a greater blood supply to any one nerve.

The manner in which the intraneural vascular pattern is established is fundamentally the same in all three nerves, and the terminal capillary meshwork is of approximately the same density in all situations. Microdissection and histologic studies have, however, revealed variations in the detailed structure of this pattern in all three

nerves which are so inconstant and irregular that no two patterns are identical. Consequently, there is no pattern which is constant or characteristic for any one nerve, while the form it will take in a nerve, or in a segment of the nerve, is quite unpredictable. These variations appear to be determined by the number and size of the arteriae nervorum, by their site of entry and mode of branching within the nerve and by the fascicular pattern of the nerve and its connective tissue framework. All these morphologic features are known to be variable. The pattern is apparently designed to provide the most effective blood supply to the peripheral nerve in terms of its anatomic structure, and the variations observed are but a reflection of the measures adopted to achieve this. From a study of the intraneural vascular pattern in all three nerves, in the same and in different specimens, it may be concluded that though a comparison of the pattern of any two nerves will reveal obvious differences, there is nothing in these differences to suggest that one receives a better or a poorer blood supply than the other.

Thus, the number and size of the arteriae nervorum, together with their distribution within the nerve, are subject to such a wide range of variation, not only in the three nerves but in the same nerve in different specimens, that on the basis of anatomic observations alone it is impossible to reach any definite conclusion regarding the relative richness of supply to the various peripheral nerve trunks. The observations demonstrate that, with regard to the three anatomic features under discussion, there are inconstant and unpredictable differences in the three nerves and in the same nerve in different specimens. There is nothing to suggest from the evidence available that such differences can in any way be interpreted as an indication of a richer or a poorer blood supply. They appear to be due to variations designed to give, under prevailing anatomic conditions, the most effective blood supply to the peripheral nerves. It is conceivable, however, that these minor structural differences and variations imposed on the basic pattern may be a manifestation of much greater functional ones; but since they are common to all three nerves, there do not appear to be any grounds for attributing differences in the reaction of these nerves to injury, mechanical or otherwise, to any specific difference in the vascular pattern.

Median Nerve in the Upper Arm and Forearm.—The size and distribution of the median artery render difficult any comparison of the blood supply of the nerve in the upper arm and that of the nerve in the forearm. The number of nutrient arteries to the nerve in the upper arm exceeds in the great majority of cases (33 out of 37 specimens) the number to the nerve in the forearm (table 5). The number of arteriae nervorum appears to be closely related to their size and to the proximity of the parent vessel to the nerve. It is suggested that the median nerve receives fewer nutrient arteries in the forearm because there is no large limb artery accompanying the nerve in this region. As already observed, this is compensated for principally by the large size of the median artery or by long descending intraneural channels. Exclusive of this artery, however, the arteries reaching the nerve in the upper arm are usually, but not invariably, larger than the arteries reaching it in the forearm.

In general, the large intraneural arterioles in the upper arm are present on or toward the surface, whereas in the forearm they are, with the exception of the median artery, usually more centrally placed. Apart from this difference, which is by no means constant, the intraneural vascular pattern is subject to such a wide range of variations from one level to another and from one subject to another that there is no pattern which is constant or characteristic for any one part of the nerve. These local differences which are observed along the entire length of the nerve are but a reflection of the measures undertaken to assure, under the prevailing anatomic conditions, the most effective blood supply to the nerve.

There is nothing to suggest, from the anatomic evidence available, that one part of the nerve receives a better or a poorer blood supply than another.

Ulnar Nerve in the Upper Arm and Forearm.—The number of nutrient arteries to the nerve in the upper arm as compared with the number to the nerve in the forearm is as follows:

No. of Arteries	No. of Specimens
Equal	3
Greater in the forearm	18
Greater in the upper arm	16

Ramage claimed, however, that the number in the forearm always exceeds that in the upper arm.

In each specimen the largest nutrient arteries are usually, but not invariably, noted in the upper arm. When, however, the size and number are studied together in the same specimen, these two morphologic features are found to bear an inverse relation to one another. With regard to the structure of the intraneural vascular pattern along the length of the nerve, the observations were identical with those recorded for the median nerve, and the same conclusions apply.

On this evidence it is impossible to assign a constantly greater blood supply to any particular segment of the nerve.

Median and Ulnar Nerves in the Forearm.—The number of nutrient arteries to the two nerves in the forearm in each specimen is shown in table 5. In the majority of specimens (31 out of 37) the number of nutrient arteries to the ulnar nerve exceeded the number to the median nerve, the difference being explained in some measure by the disposition of the large arteries relative to the two nerves in the forearm.

The size and distribution of the median artery render difficult any comparison between the blood supply of these two nerves. There appear, however, to be significant differences in the number of nutrient arteries reaching the nerves in the forearm, though the smaller number to the median nerve is usually compensated for by the large size of the median artery. With the exception of this vessel there is no significant or constant difference in the size of the nutrient arteries passing to the two nerves.

A comparison of the intraneural pattern in the two nerves gave results identical with those previously described in the three preceding sections, and the same conclusions consequently apply.

Thus, it is impossible to assign a constantly greater blood supply to any particular segment of either nerve.

Superficial Radial and Posterior Interosseous Nerves.—Comparison of the number of arteries to each nerve as observed in this investigation with the figures listed by Ramage gave the following results:

	No. of Specimens	
No. of Nutrient Arteries	This Series	Ramage's Series
Equal to the two nerves	5	7
Greater to superficial radial nerve	17	13
Greater to posterior interosseous nerve	15	4

In the present investigation neither nerve consistently received more arteries than the other, and in only a small majority of specimens did the number of arteries passing to the superficial radial nerve exceed the number to the posterior interosseous nerve. Ramage's figures indicate a higher incidence for the superficial radial nerve, though, on the basis of his methods of comparison, he gave the average number of arteries per specimen as 4.05 and 4.6 to the posterior interosseous and the superficial radial nerves respectively. However, in comparison of the blood supply of these nerves he claimed to have demonstrated that "when sections of the posterior interosseous and radial nerves are compared, it is found that the area of nervous tissues in the two is about equal, but the area of the blood vessels in the radial is three and a half times as great as the area of the blood vessels in the posterior interosseous." I have been unable to confirm this observation. A comparison of the number, size and disposition of the arteriae nervorum failed to reveal any constant or characteristic differences for the two nerves. On the contrary, an analysis of the pattern suggests that, despite the variations, the blood supply to individual nerve fibers in the two nerves is substantially the same.

SUMMARY: GENERAL FEATURES

1. Each peripheral nerve is abundantly vascularized throughout its entire length by a succession of vessels which by their repeated division and anastomosis within the nerve outline an unbroken intraneural vascular net.

2. The arteriae nervorum arise at irregular intervals from the limb arteries or their branches which establish an intimate anatomic relationship with the peripheral nerve or which, at most, are not far distant from it.

3. The vessels which supply the nerve exclusively and which take origin from the main vessel, or from one of its named branches, are called direct nutrient arteries. Opposed to this type are the nutrient arteries which, because of their origin from branches (muscular or subcutaneous) destined to supply extraneural tissues predominantly, are referred to as indirect. The former type predominate in the case of the large peripheral nerves of the limbs.

4. For each individual nerve there is a reasonably constant group of arteries which, by the nature of their anatomic disposition, are favorably situated to supply the nerve and from which the arteriae nervorum are consequently derived.

5. Despite the presence of this reasonably constant vascular pathway, both the number and the precise site of origin of the arteriae nervorum arising from the vessels composing it vary over wide limits—not only from subject to subject but on the two sides of the body.

6. There are certain regions where nerves habitually receive arteries.

7. Despite the variability in the number and site of origin of the arteriae nervorum, their disposition may be such, particularly in certain regions, that it is impossible to free a nerve from the surrounding tissues for more than a few centimeters without sacrificing some of the vessels supplying it.

8. Extensive segments of a nerve which do not receive any nutrient arteries are frequently

seen. Microscopic examination of these segments fails to demonstrate any modification of the fundamental character of the intraneural vascular pattern, the segment being nourished and the pattern maintained by large descending intraneural vessels derived from the last entering nutrient artery.

9. The number and size of the arteriae nervorum are variable morphologic features. There appears to be an inverse relation between the two.

10. Larger nerves do not necessarily receive more vessels than smaller nerves.

11. The caliber of the nutrient arteries fluctuates over wide limits. The largest artery seen measured 1 mm. in diameter.

12. The largest vessels run to the largest nerves, though the largest nerves do not invariably receive larger arteries than do smaller nerves. The largest arteries in the upper limb are present in the upper arm.

13. Both size and number must be taken into account in estimating the relative vascularity of different segments of the same nerve and that of corresponding segments of different nerves.

14. The size and the length of the nutrient arteries are independent features. The length appears to be determined by the proximity of the parent vessel—the closer the parent artery, the shorter the nutrient branch.

15. The nutrient vessels take the most direct route to the nerve and are therefore straight or gently curved.

16. Nutrient arteries, on or adjacent to the nerve they are to supply, outline a variety of patterns of distribution.

17. On entering a nerve a nutrient artery may be distributed in one of several ways.

18. The intraneural pattern is composed of arterioles, precapillaries, capillaries and venules.

19. The largest intraneural arterioles are observed on the surface of the nerve and in the interfascicular tissues, where they branch to form a series of longitudinally disposed channels of arteriolar, precapillary and capillary type.

20. There is a general tendency for the largest vessels to be situated toward the center of the nerve in the forearm and at the periphery in the upper arm.

21. The largest intraneural arterioles in the arm are usually, but not invariably, seen in the upper arm.

22. From the interfascicular arterioles finer branches pass into the perineurium and fasciculi —precapillaries predominate in the former and capillaries in the latter. These branches are also longitudinally disposed.

23. The longitudinally directed epineurial, interfascicular, perineurial and intrafascicular vessels repeatedly give off side branches, more or less at right angles, in all directions at frequent but irregular intervals. These branchlets redivide in a similar manner and finally anastomose to give a fine terminal intraneural vascular net composed of rectangular meshes disposed in the plane of the longitudinal axis of the nerve.

24. The number, size and position of the interfascicular longitudinally directed vessels vary from level to level.

25. Though the intraneural vascular pattern has the same fundamental structure in all nerves, modifications which are determined by the number, size, position and manner of branching of the intraneural arterioles are superimposed on the basic structure. Nevertheless, the disposition of the terminal intrafascicular capillary meshwork is such that the number of capillaries per unit area of fibers appears to be relatively constant, irrespective of the nerve or their position in it. It may reasonably be inferred from this that the blood supply to the individual nerve fibers is, on anatomic grounds at least, substantially the same.

26. A characteristic feature of the intraneural pattern is the considerable overlap of supply which obtains between nutrient arteries entering at different levels. This, together with the profuse anastomosis, renders it unlikely that any vessel will dominate the intraneural circulation in any particular region or segment of the nerve. The vascular pattern has significance in connection with the production of local and general ischemia of the nerve.

27. Venules are the largest venous vessels seen in or leaving the nerve.

28. The structure of the intraneural venous pattern corresponds to the arterial arrangement. Venules and arterioles, however, do not always run together, either inside or outside the nerve, while counts suggest that the number of interfascicular venules exceeds the number of arterioles.

29. Veins may leave the nerve independently of the entering arterioles.

30. The number of veins leaving the nerve does not always correspond with the number of arteries entering it.

31. The emerging veins may terminate in the principal vein or veins accompanying the neighboring artery, in muscular veins or in the venous plexus in the wall of a neighboring artery.

SUMMARY OF THE BLOOD SUPPLY TO THE MEDIAN, ULNAR AND RADIAL NERVES

The results of a study of the source, site of origin, course and distribution of the nutrient vessels to the median, ulnar and radial nerves in 37 adult arms (tables 1, 2, 3 and 4) may be summarized as follows:

The principal blood supply to the median nerve in the upper arm comes from the axillary and brachial arteries. Arteriae nervorum are occasionally received from the ulnar collateral and supratrochlear arteries.

In the cubital fossa the nerve frequently receives nutrient vessels from one or several of the arteries which are related to it in this region, namely, the termination of the brachial artery and its radial and ulnar divisions and the common interosseous, anterior interosseous and anterior ulnar recurrent arteries.

In the forearm the nerve is supplied by the radial and ulnar arteries and by the median artery, which was present and provided the main supply in 27 specimens of the 37 examined.

The ulnar nerve is accompanied throughout its course by a continuous arterial chain, derived in turn from the axillary, brachial, ulnar collateral, supratrochlear, posterior ulnar recurrent and ulnar arteries. From this system the arteriae nervorum are derived. Occasionally the profunda brachii artery and a high radial artery establish a sufficiently intimate relation to the nerve to supply it. The principal and most constant supply is from the ulnar collateral and ulnar arteries.

The radial nerve is supplied by the axillary, subscapular brachial and profunda brachii arteries in the axilla and arm before entering the spiral groove; by the profunda brachii artery while running in the groove, and, finally, from the anastomosis between the profunda and the anterior radial recurrent artery in the intermuscular furrow between the brachialis muscle, medially, and the brachioradialis and the extensor carpi radialis longus muscle, laterally. The main supply in most cases is obtained from the profunda artery.

The superficial radial nerve is supplied by the anterior radial recurrent and radial arteries or their branches. The posterior interosseous nerve is supplied by the anterior radial recurrent and posterior interosseous arteries and from the anastomosis between them in the supinator muscle, and occasionally by the anterior interosseous artery in the distal third of the forearm.

The number, size, source, site of origin and site of entry into the nerve of the arteriae nervorum are inconstant in all three nerves. In no case was the arrangement bilaterally symmetric. The range of variation observed in these morphologic features was observed to correspond closely in all three nerves.

In an analysis of the blood supply of the median, ulnar and radial nerves with a view to the detection of differences, this supply was taken to mean the arteries to the entire peripheral nerve trunk, as opposed to the individual nerve fiber, and in this connection it was assessed in terms of the size, number and intraneural disposition of the arteriae nervorum. These features are, however, so irregular and the ranges of variation for all three nerves so similar as to render difficult any comparison of them on this basis. The observations, however, appear to justify the following conclusions:

1. In the upper arm, no nerve consistently receives more nutrient arteries than another.

2. In the upper arm any nerve may receive more nutrient arteries than its fellows.

3. In the upper arm the three nerves only occasionally receive the same number of nutrient arteries.

4. In the upper arm the number of nutrient arteries passing to the radial nerve exceeds in a small majority of cases that to either the median or the ulnar nerve, while in an even smaller majority the number to the median nerve exceeds that to the ulnar nerve. The number of specimens examined was too small, however, to give data of statistical value.

5. The size of the nutrient arteries varies over substantially the same limits for all three nerves in the upper arm.

6. Usually the number of arteries to the median nerve in the upper arm exceeds that to the median nerve in the forearm. The larger number in the upper arm appears to be compensated for in the forearm, in the majority of cases, by the large size of the median artery. Except for this vessel, however, the arteriae nervorum in the upper arm are usually, but not invariably, larger than the vessels in the forearm.

7. The number of arteriae nervorum to the ulnar nerve in the forearm exceeds, in a small majority of the cases, the number reaching it in the upper arm. Usually, but not invariably, the largest nutrient arteries are found in the upper arm. When the size and the number are studied together in the same specimen, an inverse relation is observed to obtain between the two.

8. With both the median and the ulnar nerve it is more common to see the largest intraneural arterioles situated on or toward the surface in the upper arm and occupying a more central position in the forearm.

9. The size and distribution of the median artery render difficult comparisons between the arteriae nervorum to the median nerve and those to the ulnar nerve in the forearm. However, there appears to be a significant difference in the number reaching the nerves in this situation, the smaller number to the median nerve being compensated for, in the majority of cases, by the large size of the median artery. Except for this vessel, there is no significant or constant difference in the size of the arteriae nervorum to the two nerves.

10. In a very small majority of cases the number of nutrient arteries to the superficial radial nerve exceeds the number to the posterior interosseous nerve. A comparison of the size and disposition of the arteriae nervorum passing to the two nerves fails to reveal any constant or characteristic difference.

11. The manner in which the intraneural vascular pattern is established is fundamentally the same in all three nerves, and the terminal capillary meshwork is, apart from minor variations, of approximately the same density in all situations. However, the size, number, position and mode of branching of the intraneural arterioles are subject to such a considerable range of variation in all nerves that no two patterns are alike in detail. There is certainly no pattern which is constant or characteristic for any one nerve or section of a nerve. Moreover, the form the pattern will take in any particular nerve is quite unpredictable. These variations appear to be of minor significance, and there is evidence to suggest that they are to a large extent determined by the number, size and site of entry into the nerve of the arteriae nervorum, by the fascicular pattern of the nerve and by its connective tissue framework. All these morphologic features are known to be variable.

Thus, so far as the intraneural pattern is concerned there are differences not only in the three nerves but in the same nerve in different specimens, as well as at different levels of the same nerve. These differences appear to be due to minor variations in the pattern designed to provide the most effective blood supply to the peripheral nerve in terms of its anatomic structure. However, though a comparison of the intraneural vascular pattern of two nerves reveals obvious differences, there is nothing in these differences to suggest that one nerve receives a better or a poorer blood supply than the other.

12. The observations demonstrate that with regard to the three anatomic features investigated (number, size and intraneural pattern) there are inconstant and unpredictable differences in the three nerves, in the same nerve in different specimens and in different segments of the same nerve. These differences appear to be due to variation designed to give, under the prevailing anatomic conditions, the most effective blood supply to the peripheral nerve. There is nothing to suggest from the evidence available that such differences can in any way be interpreted as an indication of a richer or a poorer blood supply. It is conceivable, however, that these local structural differences and variations imposed on the basic pattern in the three nerves are a manifestation of much greater functional differences, but since they are common to all three nerves, there appear to be no grounds for attributing differences in the reaction of peripheral nerves to injury, mechanical or otherwise, to any specific difference in the intraneural vascular pattern.

It must be admitted, however, that with establishment of the structural features of the blood supply the anatomic approach has reached the limit of its usefulness. Further inquiries concerning the functional significance of the pattern and its role in various physiologic and pathologic phenomena must be settled by further investigation, preferably of an experimental nature, and not by speculations based solely on the anatomic distribution of the vessels.

Mr. L. Preston and Mr. H. Marriott prepared the illustrations and the photomicrographs respectively which accompany this article.

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INTERPRETATION OF FINDINGS IN THE CEREBROSPINAL FLUID

I. THE DEMENTIA PARALYTICA * FORMULA AND THE NECESSITY OF ITS QUANTITATIVE DIFFERENTIATION

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DEFINITION

The term "dementia paralytica formula" will here be reserved for the humoral data alone as encountered in cases of typical, not effectively treated dementia paralytica, the acute forms being disregarded, while "dementia paralytica syndrome" is used for the ensemble of clinical and humoral data. With this restriction, the dementia paralytica formula is fairly uniform. It denotes a clear and colorless aspect of the cerebrospinal fluid and the following results of the obligatory tests.

1. In the quantitative analysis of the cell picture higher numbers of mononuclear cells are encountered with dementia paralytica than with other chronic forms of neurosyphilis, say 30 to 100 cells per cubic millimeter. Qualitatively, the peculiar polymorphism of the cells, which invariably include plasma cells, is so striking that previously it was believed to be specific.

2. The total protein content also is distinctly higher with dementia paralytica than with other chronic forms of neurosyphilis. While with cerebrospinal syphilis it hardly exceeds 60 mg. per hundred cubic centimeters, with dementia paralytica it ranges from 100 to 150 mg., infrequently exceeding 200 mg. per hundred cubic centimeters.

3. The titer of the blood in the complement fixation test for syphilis lies in the same maximal range as that in cases of early secondary syphilis before treatment.

4. The titer of the cerebrospinal fluid in the complement fixation test is distinctly higher with dementia paralytica than with other forms of neurosyphilis.

5. The colloidal gold test yields the so-called characteristic curve for dementia paralytica. The terms "dementia paralytica curve" (table 1, no. 4) and "syphilitic curve" (table 1, no. 2) do not mean that the curves are supposed to be "specific for" dementia paralytica and cerebrospinal syphilis respectively, but only that they almost invariably are "encountered" with these diseases.

The five tests mentioned are obligatory; an additional feature of the dementia paralytica formula is its resistance to change with routine treatment. The question whether this resistance may be taken for granted on the basis of a single examination or must be determined by tentative routine treatment and follow-up examinations was the main reason for the quantitative classification of those formulas which is subsequently suggested.

Finally, it may be mentioned that of the numerous additional tests, particularly permeability tests, suggested for the diagnostic examination of the cerebrospinal fluid in cases of dementia paralytica, none adds essential information to that furnished by the aforementioned five obligatory tests, provided optimal methods and correct interpretations are employed. Determination of the pressure and the Queckenstedt test are of no significance.

EXPERIMENTAL STUDY

METHODS

The cell examination consists of the study of a stained sediment and the cell count in a Fuchs-Rosenthal chamber, polychrome methylene blue without acetic acid being used. Only three cell forms are differentiated: red cells and mononuclear and polymorphonuclear leukocytes. For determination of the total protein content the micro-Kjeldahl method was used in the experiments. In routine work a turbidimetric method is employed, with use of sulfosalicylic acid and a photoelectric colorimeter. The technic is so controlled that it provides a practically satisfactory substitute for the micro-Kjeldahl method. The quantitative complement fixation test for syphilis of Wadsworth, Maltaner and Maltaner [1] and the quantitative colloidal gold test of Lange [2] are employed.

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* The term "dementia paralytica formula" has been used instead of the authors' "paretic formula" for conformity with the "Standard Nomenclature of Diseases" and with the policy of the American Medical Association Press.

1. Wadsworth, A.; Maltaner, F., and Maltaner, E.: Quantitative Studies of the Complement-Fixation Reaction with Syphilitic Serum and Tissue Extract: Technic of the Practical Quantitative Test, J. Immunol. **35**:217-234, 1938.

2. Lange, C.: Methods for the Examination of Spinal Fluid, Am. J. Syph., Gonor. & Ven. Dis. **23**: 638-668, 1939.

TABLE 1.—*Various Types, Quantitative Differences and Origin of Dementia Paralytica Curves*

Serial No.	Material	Mononuclear Cells, per 3 Cu. Mm.	Total Protein, Mg./100 Cc.	Complement Fixation Titer of Blood *	Complement Fixation Titer of Cerebrospinal Fluid	Colloidal Gold Reaction †														Type of Gold Curve
						Routine Serial Dilutions										Additional Dilutions				
						1:15	1:23	1:34	1:51	1:76	1:114	1:171	1:256	1:384	1:576	1:864	1:1,296	1:1,944	1:2,916	
1	Normal cerebrospinal fluid.....	1	22	0	0	2.5	4	5	5.5 Maximum after 2 hr.	5.5 Maximum after 2 hr.	4	3.5	2.5	1	1	..	..	..	..	Normal ‡
2	Asymptomatic neurosyphilis....	14	54	55	6.3	7.5	8.5	10	12	13	14 Maximum after 2 hr.	12	8	7.5	5	..	..	..	..	Syphilitic
3	Tuberculous meningitis §.....	1,243	173	0	0	3.5	4.5	5	6	7	8.5	9.5	11 Maximum after 2 hr.	10	9	..	..	..	..	Hematogenous ‖
4	Clinically typical dementia paralytica	278	148	1,650	470	18	18	18	18	18	18	18	18 Speed maximum after 5 min.	18	18	18	18	18	16	True dementia paralytica type
5	Patient asymptomatic after routine treatment	26	47	153	19	18	18	18	18	18	18	18	14	8.5	6	..	..	..	..	Weak dementia paralytica type
6	Dementia paralytica formula after treatment	17	45	6.8	0	18	18	18	18	18	18	18	15	9.5	8	..	..	..	..	Weak dementia paralytica type
7	Clinically typical tabetic form of dementia paralytica	23	34	0	0	16	16	16	16	16	14	11	9	7.5	5	..	..	..	..	Residual dementia paralytica type
8	Dementia paralytica formula after fever therapy	1	26	7.5	2.3	12	12	12	11	9.5	9	7	5	4.5	3.5	..	..	..	..	Residual dementia paralytica type
9	Cerebrospinal fluid no. 4, after heating	..	..	..	..	6	6.5	7.5	9.5	15	17	18 Speed maximum after 5 min.	18	18	12					
						Different Serial Dilutions														
						1:1	1:1.5	1:2.3	1:3.4	1:5.1	1:8	1:11	1:17	1:26	1:38	1:58	1:86			
10	Cerebrospinal fluid no. 4 in electrolyte-poor milieu	..	..	..	..	18	18	18	18	18	15	13	11	10	9	7	5			
						Speed maximum after 5 min.														

* Titers obtained with quantitative complement fixation test.[1]

† The technic of the quantitative gold reaction was used.[2] The degrees of coagulation are determined with the gold color standard. The values range from 0; red, over violet to 10; blue, over blue-white to 20; colorless.

‡ The normal curve is characterized by maximum and strength.

§ Examination of the fluid revealed 123 polymorphonuclear leukocytes per 3 cu. mm., a cobweb-like coagulum of fibrin and tubercle bacilli.

‖ The hematogenous (meningitic) [?]) curve demonstrates passage of blood colloids into the cerebrospinal fluid, as encountered in cases of subarachnoid block and hemorrhage.

QUALITATIVE ASPECT OF THE DEMENTIA PARALYTICA FORMULA

Qualitatively, the dementia paralytica formula is characterized by the combination of a positive complement fixation reaction of the cerebrospinal fluid for syphilis and the colloidal gold curve for dementia paralytica. The grave prognostic significance of the dementia paralytica formula depends on the presence of the dementia paralytica curve, but only if technically "false dementia paralytica curves" are eliminated, which may be due either to an incorrect type definition or to an unsatisfactory p_H of the milieu.[3] On the basis of the reproducible results of the quantitative gold test, a "true dementia paralytica curve" (table 1, no. 4) is characterized by a broad plateau of complete coagulation, reaching a dilution of from 1:600 to 1:2,000. The coagulation becomes complete only after several hours, but after two hours, the usual reading time, it is almost complete. At this time the dementia paralytica curve is differentiated from all other types of curves by the absence of a prezone and a maximum. A misleading type definition is the widely adopted identification of "first zone curves" with dementia paralytica curves. It is easy to demonstrate experimentally that a true dementia paralytica curve is never a first zone curve and vice versa. In table 2, no. 4 is shown a true first zone curve, artificially elicited with a normal cerebrospinal fluid (table 1, no. 1) by bacterial contamination. Identification of this type with the dementia paralytica curve (table 1, no. 4) obviously destroys the practical value of the latter. Furthermore, in table 1, no. 8 is shown a "syphilitic first zone curve" as the residual of a dementia paralytica curve after treatment. The ensemble, particularly the almost normal total protein content, renders it obvious that prognostically this first zone curve has ceased to be a dementia paralytica curve. This quantitative definition of the dementia paralytica curve eliminates false curves due to incorrect definition.

Finally, that a true dementia paralytica curve is never a first zone curve is demonstrated by the "speed maximum," which lies in table 1, no. 4, in the dilution 1:256, and not in the first zone. The speed maximum is indicated by the dilution exhibiting the maximum speed of coagulation; in other types of neurosyphilis it is fairly identical with the maximum read after two hours. The speed maximum for the dementia paralytica curve disappears after about five minutes, because in a broad range of complete coagulation quantitative differences are bound to disappear finally. To sum up, the adequate utilization of the formula encountered with dementia paralytica requires a qualitatively and quantitatively correct definition of the dementia paralytica curve, as given here. To call a true dementia paralytica curve (table 1, no. 4) incorrectly a "first zone curve," as will be shown subsequently, is only a comparatively harmless misnomer. However, the identification of the true "first zone curve" (table 2, no. 4) with the dementia paralytica curves leads to serious trouble.

The second part of the qualitative aspect of the dementia paralytica formula concerns the question whether the difference between the curve for dementia paralytica and the curve for syphilis is only a difference of degree, as is almost generally believed, or one of kind. The experimental demonstration of the "dementia

TABLE 2.—*Telescoped and False Dementia Paralytica Curves*

Serial No.	Material	Technic	Various Serial Dilutions										Type of Curve
		Dilutions	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:500	1:1,000	
1	Dementia paralytica cerebrospinal fluid (table 1, no. 4)	Mastic [7]	4	5	5	5	5	5	4	2	1	0	Telescoped mastic curve 1/30 breadth of curve in table 1, no. 4
		Dilutions	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	1:2,500	1:5,000	
2	Dementia paralytica cerebrospinal fluid (table 1, no. 4)	Original colloidal gold test [6]	5*	5	5	5	5	5	4	3	1	0	Shorter gold curve, 1/6 of curve in table 1, no. 4
		Dilutions	1:15	1:23	1:34	1:51	1:76	1:114	1:171	1:256	1:384	1:576	
3	Tuberculous cerebrospinal fluid (table 1, no. 3)	Quantitative colloidal gold test, buffer p_H 6.2	18	18	18	18	18	17	17	17	16	15	False dementia paralytica, due to inadequate p_H
4	Normal cerebrospinal fluid (table 1, no. 1), after bacterial contamination	Quantitative colloidal gold test, correct p_H 7.4	5	5	5	4.5	4.5	4	3	2	1.5	1	Nonsyphilitic first zone curve

* In numbers 1 and 2 the degree of coagulation was subjectively appraised; 5 means complete coagulation. In numbers 3 and 4 the gold color standard was used.

3. Lange, C., and Harris, A. H.: The Significance of the p_H in the Gold Reaction, J. Lab. & Clin. Med. **29**:970-975, 1944.

paralytica substance" shows that the peculiar character of the dementia paralytica curve is due to a radical qualitative difference.

After the cerebrospinal fluid in a case of dementia paralytica (table 1, no. 4) was heated for ten minutes at 70 C., the colloidal gold curve (table 1, no. 9) lost its dementia paralytica character and became more similar to the type obtained with tuberculous meningitis. This experiment suggests that heating inactivates a substance which is mainly responsible for the dementia paralytica character of the curve. This substance has not as yet been isolated, but it seems to be an abnormal pseudoglobulin-like compound, which is heat sensitive and nondialyzable; it is not removed with the euglobulins but is precipitated by 50 per cent saturation with ammonium sulfate. This substance is abnormal in that, contrary to the behavior of normal globulins in the cerebrospinal fluid, it coagulates colloidal gold in an electrolyte-poor milieu. Under these conditions, fortunately it can be demonstrated without any interference by other globulins. In order to maintain the same p_H as in the routine gold reaction, the cerebrospinal fluid in a case of dementia paralytica (table 1, no. 4) was dialyzed against a hundredth-molar solution of the usual phosphate buffer [2] of p_H 7.4. (Dialysis against distilled water would produce a p_H of about 5.7 to 6.0, with entirely different results.) The partially precipitated euglobulin after dialysis was removed and the supernatant fluid tested. A hundredth-molar buffer solution was used as diluent, and the acid "citrate gold" sol was neutralized to p_H 7.4 shortly before use. In this electrolyte-poor milieu, at p_H 7.4, in which neither normal globulins nor the heated cerebrospinal fluid of a patient with dementia paralytica has any effect on the colloidal gold solution, the curve shown in table 1, no. 10, was obtained. The curve exhibits a broad plateau of complete coagulation without a prezone. It must be taken into account that the strength of this reaction is considerably reduced by the low electrolyte concentration. As yet this reaction in an electrolyte-poor milieu at p_H 7.4 has been demonstrable only in cerebrospinal fluids yielding a curve of dementia paralytica type. The demonstration of the "dementia paralytica substance" provides the conclusive experimental differentiation of "chemically specific" and technically false dementia paralytica curves.

The gold reaction differentiates protein patterns which on the whole are etiologically nonspecific. In the dementia paralytica curve the nearest approach to etiologic specificity is reached, but still curves of this type are encountered in 1 and 2 per cent of cases of nonsyphilitic conditions. There remains, therefore, the establishment of its general pathogenic interpretation, i. e., the common causal factor that produces the dementia paralytica curve with etiologically different conditions. The hematogenous (meningitic) curve is encountered in cases of acute exudative inflammation, associated with polymorphonuclear cells, while the presence of fibrin demonstrates increased permeability. The "syphilitic curve," however, is encountered with chronic nonexudative inflammation, associated with mononuclear cells and normal permeability. Accordingly, the syphilitic curve seems to indicate chronic proliferative inflammation, as encountered with syphilis and multiple sclerosis, in contrast to bacterial infections. The dementia paralytica curve appears sporadically in association with advanced stages of epidemic encephalitis or other neurovirus infections and regularly with acute progressive stages of multiple sclerosis and with dementia paralytica, i. e., with forms in which extensive parenchymatous degeneration takes place. This is the reason that the designation "parenchymatous curve" [4] was suggested instead of "dementia paralytica curve," or the incorrect term "first zone curve." The term "dementia paralytica curve," according to the preceding unobjectionable definition, connotes "as encountered in cases of dementia paralytica." The term "parenchymatous curve" seems, at first, much better, since it is based on a sound pathogenic interpretation. However, the fact is not expressed that in cases of typical tabes, a parenchymatous form of neurosyphilis, a curve of this type is not encountered, a fact which accordingly indicates not simply parenchymatous degeneration, but "extensive parenchymatous degeneration as encountered with dementia paralytica." In short, some reference to dementia paralytica is hardly avoidable.

To sum up, the qualitative difference between the dementia paralytica and the syphilitic curve, or any other type, depends on the presence of an abnormal pseudoglobulin-like substance, indicating extensive parenchymatous degeneration and as yet detectable only by the colloidal gold reaction. These experimental facts explain the grave prognostic significance of the dementia paralytica curve, irrespective of the etiologic factor, which is to be determined on the basis of the syndrome as a whole.

QUANTITATIVE ASPECT OF THE DEMENTIA PARALYTICA FORMULA

In the quantitative aspect of the dementia paralytica formula, three parts must be considered: (1) the demonstration of syphilitic

4. Thompson, L. J.: Interpretation of the "Paretic Curve" in Lange's Colloidal Gold Test, Arch. Neurol. & Psychiat. **5**:131-145 (Feb.) 1921.

reagins, providing not only the etiologic diagnosis but, by the fixed or recurring reaction of the blood, a warning to examine the cerebrospinal fluid; (2) signs of degeneration, providing the prognostic differentiation of neurosyphilis, and (3) signs of inflammation, indicating the "activity of neurosyphilis and its amenability to specific treatment." After the specific diagnosis of neurosyphilis is established, the signs of degeneration and inflammation are of predominant significance. Before the consideration of details, it must be determined which parts of the dementia paralytica formula provide information about inflammation or degeneration and their quantitative degree.

The signs of degeneration, either clinical or humoral, determine the prognosis and the intensity of therapy, which varies in cases of neurosyphilis from routine therapy to the modern treatment of dementia paralytica. Clinical and humoral signs of degeneration are in most respects different and supplement each other. A dementia paralytica curve indicates that extensive degeneration is still going on, while in cases of a burnt-out process clinical signs of degeneration survive the active stage, i. e., the inflammatory process. Vascular insults may occur years after the primary inflammation has come to a standstill, as indicated by a normal cerebrospinal fluid. Tabetic signs of degeneration do not necessarily indicate "active neurosyphilis, amenable to treatment." Humoral signs provide no localization, while clinical degenerative signs may assume a specific character, through their topographic arrangement alone. With typical tabes no dementia paralytica curve is observed, in contrast to clinical signs and symptoms of parenchymatous degeneration or irritation. With tabes the clinical manifestation is more sensitive; the colloidal gold test is unable to detect such low degrees of degeneration. If extensive degeneration, as indicated by the dementia paralytica curve, takes place in "silent areas," no clinical manifestation can be expected. Humoral signs of degeneration may precede clinical manifestations by many years, a fact which obviously is significant from the standpoint of prevention. These considerable differences between clinical and humoral signs of degeneration are often overlooked.

The presumptive effect of therapy depends on the ratio of inflammation to degeneration, in which the degree of inflammation determines the "activity" of the process. It is well recognized that in cases of untreated dementia paralytica a low cell count, indicating torpid inflammation and an unsatisfactory defense mechanism, if associated with severe signs of degeneration, renders the prospect of therapy particularly unfavorable. In this connection two questions arise: (1) What signs of inflammation are available? and (2) Does the absence of such signs exclude "active neurosyphilis, amenable to specific treatment"?

First, the primary chronic inflammation in the central nervous system is inaccessible to clinical diagnosis as long as it is uncomplicated by parenchymatous irritation or degeneration. Only humoral signs are available. In cases of chronic neurosyphilis, the number of cells in the cerebrospinal fluid provides a quantitative expression of the inflammation in the meninges and the perivascular spaces because, under conditions of normal permeability, the pleocytosis must be of local origin.[5] Of the same significance is the increase in the total protein, which is caused by the lysis of the dead cells, shed into the cerebrospinal fluid. It will become clear subsequently why in the dementia paralytica formula an accurate determination of the total protein concentration provides the best standard for the degree of inflammation, of the "activity" of the process.

Secondly, it is controversial whether a normal cerebrospinal fluid excludes "active neurosyphilis." No agreement can be expected as long as the "syndrome of normality" is based on unsatisfactory or semiquantitative methods, and the presence of "activity" on possibly persistent clinical signs of degeneration (tabes). There is no evidence that "active neurosyphilis," connoting inflammation plus amenability to specific therapy, may persist anywhere in the central nervous system without eliciting demonstrable changes in the cerebrospinal fluid via the Virchow-Robin spaces, as with any hemorrhage. The alleged occurrence of a normal cerebrospinal fluid with "active neurosyphilis" seems to be based on the observation of the association of a normal cerebrospinal fluid with (persistent) clinical degenerative signs. That this apparent discrepancy between clinical signs of degeneration and a normal cerebrospinal fluid is never encountered in early stages of the infection suggests that it occurs only in cases of the burnt-out process. In short, the "syndrome of normality" (table 3, no. 4) renders the diagnosis of "active neurosyphilis, amenable to treatment," improbable, particularly in later stages of the infection.

With respect to the quantitative differences in dementia paralytica formulas, as yet only the changes encountered in cases of the typical, untreated disease have been considered, which are characterized by the strongest reactions given by

5. Lange, C.: Lumbalpunktion und Liquordiagnostik, in Kraus, F., and Brugsch, T.: Spezielle Pathologie und Therapie, Berlin, Urban & Schwarzenberg, 1923, vol. 2, pp. 435-686.

any of the forms of neurosyphilis and by a rough parallelism of the various elements, which is one of the most distinctive features of the cerebrospinal fluid in this disease. Today, cases of the untreated disease are infrequent, and the available material consists predominantly of cases of dementia paralytica or questionable "predementia paralytica" in which more or less treatment has been received. In the course of treatment the aforementioned maximal strength and parallelism disappear, and three steps of "dissociation" may be observed (table 3). 1. The number of cells is reduced out of proportion to the remaining elements, except during exacerbations. 2. The complement fixation reaction of the cerebrospinal fluid occasionally may become negative at a time when the total protein concentration and the colloidal gold reaction are still distinctly abnormal, particularly in cases of the tabetic form of the disease. 3. In the last stage, when the colloidal gold curve approaches the normal, there may appear either a residual dementia paralytica curve (table 1, no. 8), suggesting residual degeneration without considerable inflammation, or a weak syphilitic curve, suggesting residual inflammation without extensive degeneration. Accordingly, a normal cell picture and a negative reaction to the complement fixation test are less valuable for the demonstration of cure than the total protein content, as the main indicator of inflammation, or the colloidal gold curve, as the main indicator of degeneration. The last two tests demonstrate quantitative differences throughout the whole range (table 3), from the strongest dementia paralytica formula down to "normality."

One may analyze now the results of the single tests in their quantitative relation to the three categories of information that the dementia paralytica formula provides: The first effect of therapy is a notable decrease in the number of cells, particularly when the dementia paralytica formula shows a maximal degree of pleocytosis. This cytolysis produces dissolved proteins and a fleeting increase in the total protein, the complement fixation titer and the colloidal gold reaction. Now, under conditions of (almost) normal permeability, the removal of this cytogenous protein is a far slower process than the cytolysis itself, as is well known from the study of hemorrhages.[5] This circumstance is of considerable technical significance; in cases of treated neurosyphilis the total protein concentration, being more persistent and accurately determinable, is far superior to the number of cells as an indicator of the inflammatory process, the "activity of the neurosyphilis." It is obvious that this situation requires a sufficiently accurate determination of the total protein concentration, for which the current qualitative or semiquantitative tests for globulin are unsatisfactory.

An optimal complement fixation test of the cerebrospinal fluid for syphilis is on the whole superior to most flocculation tests. However, even if the most sensitive complement fixation test is used, a negative reaction of the cerebrospinal fluid (table 1, no. 6) is of as little value as the cell picture in the demonstration of cure, which is to be based on the nonspecific total protein content and the colloidal gold reaction. In fact, for some purposes the complement fixation test of the blood is more important, the value however, depending largely on the method used. In the literature, from 10 to 19 per cent of negative reactions of the blood are reported in association with the "dementia paralytica formula" and from 30 to 48 per cent, in cases of neurosyphilis with a positive complement fixation reaction of the cerebrospinal fluid. The results of the quantitative complement fixation test [1] are strikingly different in this respect. Of cases of neurosyphilis in which a dementia paralytica formula was not exhibited but a positive complement fixation reaction of the cerebrospinal fluid was obtained, only 3 to 5 per cent yielded a negative reaction of the blood, even including cases of the later stages. In no case in which the dementia paralytica formula was obtained was the reaction of the blood negative, but here the elimination of a "false dementia paralytica curve" was probably more significant than the technical differences of the complement fixation test. Although the percentages previously cited are by no means conclusive, the fact that the quantitative complement fixation test [1] secures a considerably higher percentage of positive reactions of the blood in cases of neurosyphilis seems to be beyond doubt. This difference in the results of various technics usually is disregarded in the evaluation of methods, although it is most significant for the prevention of neurosyphilis. If, actually, optimal methods invariably secure a positive reaction of the blood in the presence of a dementia paralytica formula for the cerebrospinal fluid, all these cases of severe neurosyphilis could be detected by a routine examination of the blood, leading to examination of the cerebrospinal fluid and early administration of optimal therapy.

This technical factor is likewise important in the differentiation of the dementia paralytica formula from the "syndrome of multiple sclerosis," as encountered in acute progressive stages. The humoral part of the latter consists of negative complement fixation reactions of the blood and the cerebrospinal fluid for syphilis combined with a dementia paralytica curve; the latter invariably is a "weak dementia paralytica

curve," such as that indicated in table 1, no. 5 or 6. A similar humoral picture may be encountered with typical tabetic dementia paralytica (table 1, no. 7). It is obvious that the value of a negative, i. e., in any case, less conclusive, element in the formula largely depends on the previously analyzed ability of various methods to secure positive reactions of the blood in cases of neurosyphilis.

The colloidal gold reaction, as stated before, is too insensitive to detect the parenchymatous degeneration in cases of typical tabes. For this quantitative study it is necessary to select the most sensitive technic, of course, without its chemical specificity for the "dementia paralytica substance" being jeopardized. Since the dementia paralytica curve is characterized by a broad plateau of complete coagulation, the relative sensitivity of various "colloid reactions" may be roughly determined by the breadth of this plateau. The same dementia paralytica type of cerebrospinal fluid was first examined (table 1, no. 4) by the quantitative colloidal gold test.[2] The result of the original gold test,[6] in which "formol gold" was used, is shown in table 2, no. 2, and the result of an optimal mastic test,[7] in table 2, no. 1. The superior sensitivity of the quantitative colloidal gold test, due to the selection of an optimal "citrate gold" sol,[8] is manifest. The plateau with the "formol gold" test is one-sixth, and the plateau with the mastic test one-thirtieth, that for the quantitative colloidal gold test. The "telescoped" curves obtained with the mastic test indicate an absolute lack of sensitivity; a satisfactory prognostic differentiation of neurosyphilis cannot be based on the results of such a method, the even more unsatisfactory benzoin test being disregarded.

The chemical specificity of the dementia paralytica curve may today be controlled by the demonstration of the "dementia paralytica substance." "False dementia paralytica curves" are chiefly due either to the confusion with "first zone curves," already discussed, or to an unsatisfactory technic, particularly a too low p_H of the milieu. A comparison of table 1, no. 3, with table 2, no. 3, shows that a change in the p_H from 7.4 to 6.2 transforms a correct hematogenous (meningitic) curve into a false dementia paralytica curve.[3] Every modification of the colloidal gold reaction which uses acid colloidal gold solution without neutralization, or tries to compensate for lack of sensitivity by the addition of acid, is bound to yield "false dementia paralytica curves." In the quantitative colloidal gold reaction, the sensitivity is secured by the selection of an optimal colloidal gold solution,[8] and the specificity, by maintaining the obligatory p_H of 7.4 by use of a strong buffer as a diluent; the reproducibility is controlled by the use of an adequate test fluid. All these factors are made possible only by the use of a gold color standard. Tables 1 and 3 show that the results of the quantitative gold test run fairly parallel with the total protein concentration throughout the quantitatively different types of the dementia paralytica formula.

TABLE 3.—*Quantitative Classification of Dementia Paralytica Formulas*

	Types	Percentage in This Study	Total Protein, Mg. per 100 Cc.	Colloidal Gold Reaction	Complement Fixation Reaction of Blood	Complement Fixation Reaction of Cerebrospinal Fluid	Cell Picture
1	True dementia paralytica formula	32	About 100-150	True dementia paralytica curve (table 1, no. 4), complete coagulation up to dilutions of 1:600 to 1:2,000	Invariably strongly positive	Strongly positive, weaker than blood titer	In cases of untreated disease strong mononucleosis with polymorphism
2	Weak dementia paralytica formula	42	50-100	Complete coagulation up to dilutions of less than 1:500 (table 1, nos. 5 and 6)	Strongly positive	Sporadically negative (table 1, no. 6)	After treatment of little value, except in exacerbations
3	Residual dementia paralytica formula	26	25-50	Short plateau of incomplete coagulation (table 1, nos. 7 and 8) or atypical forms	Sporadically negative, before reaction of cerebrospinal fluid became normal	Often weakly positive, even if total protein content almost normal	After treatment of little value, except in exacerbations
4	Normal formula	..	15-25	Normal curve (table 1, no. 1)	Negative	Negative	0-2 mononuclears per 3 cu. mm.

QUANTITATIVELY DIFFERENT TYPES OF THE DEMENTIA PARALYTICA FORMULA

After the preceding technical and theoretic analysis, table 3 is self explanatory. The neces-

6. Lange, C.: Die Ausflockung kolloidalen Goldes durch Zerebrospinalflüssigkeit bei luetischen Affektionen des Zentralnervensystems, Ztschr. f. Chemotherap. **1**: 44-78, 1912.

7. Emanuel, G., and Rosenfeld, H.: Die Emanuelsche Mastixreaction der Rückenmarksflüssigkeit in neuer Form, Klin. Wchnschr. **6**:1375-1378, 1927.

8. Lange, C., and Harris, A. H.: A Citrate Gold of Optimal and Reproducible Sensitivity for Use in the Colloidal Gold Reaction: Its Preparation and Control, Am. J. Pub. Health **34**:1087-1092, 1944.

sity of differentiating these types of the dementia paralytica formula is as obvious as the fact that their differentiation requires optimal quantitative methods. Type 1 is well defined as the maximal and fairly uniform strength encountered with dementia paralytica; type 3 is as well defined by an "almost normal" total protein content. The lines of demarcation of type 2 are of necessity arbitrary. The percentages, calculated for the various types, are not assumed to be accurate, in view of the fact that the lines of demarcation of the types are not well defined and that inadequate data frequently accompany specimens. However, they seem to be sufficiently accurate to point out that only about one third of the dementia paralytica formulas, when they are detected and are to be evaluated for therapeutic considerations, are "true dementia paralytica formulas, as encountered with dementia paralytica."

COMMENT

Contrary to the predominantly qualitative concept of the dementia paralytica formula, Stokes [9] takes account of the strength of the curve for the disease in the ensemble of the dementia paralytica formula, which he calls the "red flag" of the disease. He states that fluids "in which the first-zone gold sol reaction is of great intensity, are almost invariably paretic." [9a] From his data, it is obvious that he means a true dementia paralytica curve, according to the previous definition. In addition, he states: [9b]

> Notwithstanding this necessity for cautious interpretation, the first-zone colloidal test in its presence or absence is the one most important single prognostic item in the spinal fluid examination with respect to syphilis.

In determination of the protein, Stokes still uses a qualitative test for globulin but points out that an accurate determination of the total protein might be preferable, which, indeed, in the preceding analysis was found to be the optimal standard for the quantitative differentiation of formulas of the dementia paralytica type.

Moore,[10] using an obviously different colloidal test and no quantitative specification, drew the following conclusion, to some degree different:

> The paretic formula . . . especially if treatment efforts fail to effect significant improvement, is of serious prognostic import. It indicates definitely that the patient is in danger of developing further neurologic progress which is particularly likely to be tabetic or paretic in nature.

9. Stokes, J. H.: Modern Clinical Syphilology, ed. 3, Philadelphia, W. B. Saunders Company, 1944, (*a*) p. 119; (*b*) p. 116.

10. Moore, J. E.: The Modern Treatment of Syphilis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1943, p. 368.

The experience of one of us (C. L.) agrees in principle with that of Stokes. Only, while Stokes bases the quantitative specification of the dementia paralytica formula on more general terms, we wish to stress the necessity of basing the quantitative differentiation on optimal quantitative methods, yielding reproducible results, particularly in the determination of the total protein and the colloidal gold reaction. The controversial question whether the dementia paralytica formula, or, rather, the "true dementia paralytica formula," indicates dementia paralytica or, in early asymptomatic stages, "potential dementia paralytica," can, for obvious reasons, never be conclusively solved. From a practical standpoint, however, the question may be considered academic. The immediate problem, after a dementia paralytica formula indicating extensive parenchymatous degeneration is detected, concerns the selection of the adequate intensity of therapy in order to stop further progress of the disease, irrespective of whether or not it is assumed that the condition is dementia paralytica.

This practical task being considered, the question arises, as mentioned in the introduction, whether in the presence of a dementia paralytica formula the resistance to less intense treatment can be predicted from a single examination. Stokes's answer was: "No time for 'neo' now. Tryparsamide? Fever?" [9a] But this situation actually refers to a quantitatively defined formula for dementia paralytica. If Moore seems to be therapeutically more conservative, it must be considered that he speaks of a dementia paralytica formula generally without quantitative specification. The importance of wasting no time or money on presumably inadequate treatment after a dementia paralytica formula has been demonstrated can hardly be overrated. On the other hand, it seems beyond doubt that the selection of adequate therapy must take into account the striking quantitative differences of dementia paralytica formulas.

Without formulation of any detailed conclusions, it may be of value to attempt to elucidate the therapeutic situation by a few representative cases selected from earlier or asymptomatic stages.

Case 1.—The cerebrospinal fluid was first examined fifteen months after infection, and after eight months of routine treatment had failed to yield a negative reaction of the blood. A "true dementia paralytica formula" was found, as indicated quantitatively by the total protein content of 132 mg. per hundred cubic centimeters, while the other results were in the same maximal range. In this case, the dementia paralytica formula was complete in that it included even the demonstration of resistance to routine treatment, so that the therapeutic decision was the simplest possible.

CASE 2.—A routine premarital blood test yielded a positive reaction for syphilis of a very high titer. The cerebrospinal fluid exhibited the strongest dementia paralytica formula, i. e., a total protein content of 178 mg. per hundred cubic centimeters. The question is whether it is at all sensible to try routine treatment under these conditions.

CASE 3.—Data such as are presented in table 1, no. 5, deserve most attention because of their frequency. With the use of a satisfactory method of determination of the total protein and the colloidal gold test, there cannot be the slightest doubt that although the formula is qualitatively of dementia paralytica type, it is not a dementia paralytica formula "as encountered with dementia paralytica," in contrast to the formulas in cases 1 and 2. The majority of the weak dementia paralytica formulas encountered in our experience are detected when the cerebrospinal fluid is submitted "for control of treatment," which generally means routine treatment. The main difficulty in cases of this type is to determine whether the inferior strength of the formula is the effect of routine treatment, so that a factor in the dementia paralytica formula, particularly essential for therapeutic considerations, is lacking, namely, the resistance to routine treatment. In an individual case, only follow-up study can determine whether the strength of the formula is progressive or regressive. In later stages of the infection regression seems to be the rule, so that the "weak dementia paralytica formula" does not seem to be the true formula with regard to the factor of greatest practical importance, namely, the resistance to treatment. In short, the weak dementia paralytica formula, constituting the largest number of formulas for this disease obtained in this laboratory, is distinctly different from the true dementia paralytica formula, "as encountered with dementia paralytica."

CASE 4.—The "residual dementia paralytica formulas" (table 1, no. 8) demonstrate beyond doubt that the qualitative concept of the dementia paralytica formula is unsatisfactory, since it includes without differentiation the strongest pathologic changes and almost normal quantitative factors.

To sum up, if a dementia paralytica formula is detected, particularly in a case of asymptomatic neurosyphilis, the main task consists in immediate selection of the most adequate form of therapy. For this decision, a consideration of the quantitatively different types of the dementia paralytica formula is indispensable.

SUMMARY AND CONCLUSIONS

The formula as encountered in cases of typical untreated dementia paralytica is one of the most distinctive and important diagnostic findings concerned with the cerebrospinal fluid. It provides the main prognostic differentiation of neurosyphilis, possibly in early asymptomatic stages. Qualitatively, it is characterized by the combination of a positive reaction for syphilis and a dementia paralytica (parenchymatous) colloidal gold curve and, quantitatively, by a strength of all reactions which is unrivaled by other forms of neurosyphilis. From the practical standpoint, its varying resistance to specific therapy is most significant.

A correct evaluation of the dementia paralytica formula requires the elimination of "false dementia paralytica curves," due either to confusion with first zone curves or to an unsatisfactory p_H of the milieu. The qualitative differentiation of the dementia paralytica curve from all other types of curves is based on the presence of an abnormal pseudoglobulin-like "dementia paralytica substance," indicating extensive parenchymatous degeneration. This explains the grave prognostic significance of any dementia paralytica curve, irrespective of whether it is encountered as an element of the dementia paralytica formula or as part of the "syndrome of multiple sclerosis."

When quantitatively standardized methods are used, particularly in the determination of total protein and in the colloidal gold test, striking quantitative differences in dementia paralytica formulas are demonstrable. Of cerebrospinal fluids that were submitted for control of treatment, only about one third yielded "true dementia paralytica formulas, as encountered with dementia paralytica," and two thirds were notably weaker. Whether a true dementia paralytica formula, detected in the early asymptomatic stage, means prospective development of the disease cannot be determined; besides, the question is comparatively irrelevant. At the moment of the detection, the problem of the presumptive resistance to antisyphilitic treatment is paramount, since it determines the selection of adequately intense therapy. The direct determination of this resistance by follow-up examinations may involve a waste of time and money.

Without premature conclusions, the results of quantitative methods suggest that the resistance to antisyphilitic treatment roughly parallels the strength of the dementia paralytica formula, which is best expressed by the total protein concentration. It is suggested that the current qualitative concept of the dementia paralytica formula be abandoned and that the connection between this formula and its varying resistance to therapy on the basis of quantitatively different types be studied.

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PREFRONTAL LOBOTOMY IN TREATMENT OF CHRONIC PSYCHOSES

WITH SPECIAL REFERENCE TO SECTION OF THE ORBITAL AREAS ONLY

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For the past decade the surgical approach to the treatment of mental disease has been attaining increasing prominence [1] and recognition [2] in this country. As an attack on the intact brain tissue for the relief of mental symptoms, it is comparable to differential section of the posterior trigeminal root for the relief of intractable physical pain.[3] The first, and isolated, attempts at surgical treatment of mental derangements can be traced back to Burckhardt's [4] unilateral multiple cortical excisions (1890), to Puusepp's [5] unilateral subcortical section of the centrum semiovale in the frontal region of the dominant hemisphere (1906 to 1910) and to Ody's [6] unilateral lobectomy (1936).

The recent discoveries in the field of neurophysiology [7] and psychopathology [8] were put into use by Egas Moniz and Almeida Lima [9] (1935) on the European continent. Freeman and Watts,[10] in this country, have introduced and improved the method of bilateral prefrontal coring by the substitution of bilateral subcortical transection of the four prefrontal quadrants in the plane of the coronal suture (bilateral prefrontal lobotomy).

Clinical reports [11] and suggestions [12] in the literature indicate that effective therapeutic results might be obtained by limiting the transection of the prefrontal lobe to the orbital areas alone. Such a procedure, if effective, would restrict the extent of destruction, as well as the postoperative sequelae and defects. We therefore decided to limit our operation to section only of the orbital region, or lower quadrants of the frontal lobe. The results obtained from this modified procedure form the basis of the present report.

METHOD

The surgical procedure was carried out with the patient under anesthesia induced with solution of tribromoethanol U. S. P. After preparation of the operative field, a point 3 cm. posterior to the lateral rim of the orbit and 5 cm. above the zygomatic process was marked out with methylrosaniline chloride.[10] A vertical incision of about 2 cm. was then made in the plane of the coronal suture and carried down to the bone. A perforator burr hole was made in the bone through the suture line at the point indicated, and the dura was opened in a cruciate fashion. After the surface of the cortex had been coagulated, a ventricle needle was introduced through a stab incision in the avascularized area in a direction at right angles to the sagittal plane in order to locate the tip of the ventricle. Occasionally additional bone had to be rongeured away anteriorly in order to reach the tip of the anterior horn. A Sachs dural dissector was introduced along the needle in front of the ventricle to a distance of 5 cm. from the surface of the skull. A cut was made in the plane of the coronal suture, the incision beginning at the level of the burr hole and being

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A preliminary account of this investigation was read at a meeting of the St. Louis Society of Psychiatry and Neurology in January 1944.

From the Department of Neuropsychiatry (Dr. Hofstatter) and the Department of Neurosurgery (Dr. Smolik), Washington University School of Medicine, and the City Sanitarium (Dr. Busch).

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directed downward. The area above the burr hole was left intact. After the section a catheter was introduced, and irrigation with warm saline solution was carried out until the return was clear. In a few instances iodized poppyseed oil was injected to demarcate the plane of the section (figure). Closure was made in layers with silk. A similar procedure was carried out on the opposite side. The patients were routinely restrained for three days to prevent their pulling at the dressing.

CLINICAL MATERIAL

In this series, 45 patients at the City Sanitarium have been operated on since May 1942. Thirty patients of this series were studied for over twelve months after operation. In the latter group, the first 8 patients had the unmodified operation described by Freeman and Watts, and the next 22 patients had the modified operation, as here described.

These 30 patients had been mentally ill from one to twenty-seven years, the average duration being ten years, and had been institutionalized from one to twelve years, with an average period of three and one-half years. Many of these pateints showed not only social maladjustment but antisocial behavior on a noisy, combative and destructive level. The majority (85 per cent) had received various forms of shock therapy (insulin, metrazol, electric shock and nitrous inhalation), the average number of treatments being thirty-one (table 1) with no, or only transient, amelioration of symptoms. In general, the outlook for these patients as to remission or recovery was poor, and any postoperative change which occurred could be regarded as the result of the operation. The indications for operation were the chronicity and malignancy of the mental processes, the pronounced antisocial behavior, the suicidal tendencies and the failure to respond to any of the known treatments.

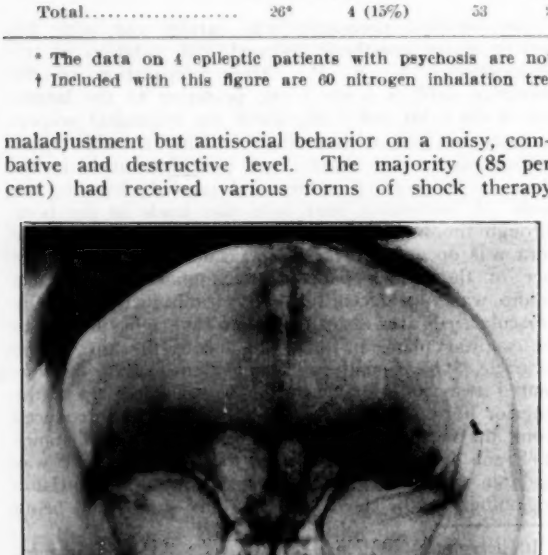
RESULTS

The distribution of and results for patients subjected to prefrontal lobotomy are outlined in table 2 and arranged according to psychiatric diagnosis and surgical method used. Three patients had affective reaction types; 1 patient, an obsessive-compulsive state; 2 patients, neurasthenia; 4 patients, epilepsy with psychosis, and 20 patients, that is, 66 per cent, schizophrenia.

TABLE 1.—*Data on Unsuccessful Preoperative Shock Treatment of Patients Who Underwent Section of the Orbital Area*

		Insulin		Metrazol or Electric Shock Treatment		Insulin and Metrazol or Electric Shock Treatment		Totals	
Disease	No. of Patients Treated	No. of Patients Treated	Average No. of Treatments	No. of Patients Treated	Average No. of Treatments	No. of Patients Treated	Average No. of Treatments	No. of Patients Treated	Average No. of Treatments
Affective reaction types	3	.....	..	3 (100%)	12	.....	..	3 (100%)	12
Obsessive tension states	1	.....	..	1 (100%)	7	.....	..	1 (100%)	7
Schizophrenias	20	3 (14%)	62	14 (70%)	28	1 (5%)	175†	16 (80%)	36
Psychoneuroses	2	1 (50%)	26	2 (100%)	15	1 (50%)	36	2 (100%)	19
Total	26*	4 (15%)	53	20 (80%)	23	2 (7.5%)	62	22 (85%)	31

* The data on 4 epileptic patients with psychosis are not included in the computation.
† Included with this figure are 60 nitrogen inhalation treatments.



Anteroposterior roentgenogram of a patient with catatonia after bilateral section of the orbital quadrants, showing distribution of the iodized poppyseed oil in the area of the section. The patient had been ill three and a half years and was now "much improved."

We considered the condition as "much improved" when the patient was able to resume his social activities and to return to his former level of occupation, as "improved" when the patient made a definitely better institutional adjustment and was assigned responsibilities which he had been incapable of assuming before the operation, as "slightly improved" when the patient's conduct and changes in behavior were such that nursing and custodial care were reduced and transfer to quieter halls and to a pleasanter environment was facilitated and as "not improved," when the patient showed no change in his behavior.

Two of the 3 patients with affective reaction types showed much improvement and were discharged. Both had depression with agitation. The condition of the third, with a chronic manic state, improved, and she was returned to her family.

One patient with obsessive-compulsive neurosis had a typical history dating from childhood,

with increasing symptoms during the years prior to institutionalization. After operation the compulsive activities gradually subsided. The patient was able to take a war job, in addition to the responsibilities in her home, and divorce proceedings instituted prior to her hospitalization were dropped by her husband.

Two neurasthenic patients, with several admissions to the institution, could not adjust on the outside before the operation. Their numerous somatic complaints progressively decreased after the operation. A somatic delusion which altered one patient's body image also disappeared. The other patient was discharged, became pregnant and is adjusting normally to the pregnancy, though she had formerly dreaded this possibility.

Four patients suffering from epilepsy with psychosis displayed sullenness, irritability, noisiness and violence as their common features. One patient responded to disturbing auditory hallucinations of an immoral nature with violent attacks on the environment. Her hallucinations subsided after the operation, but her seizures continued at about the same frequency. Her tendency to blame others for her difficulties is still present to some extent but does not now interfere with her adjustment on the outside as a housemaid. The other 3 patients have shown improvement and are now helpful and cooperative in the ward; however, shortly before the onset of their menses and of their epileptic seizures, they go through periods of increased irritability, the degree of which is less intense than before.

The schizophrenic group, table 3, comprised 2 patients with hebephrenia, 4 with catatonia and 14 (i. e., 70 per cent) with paranoia. Seven patients (30 per cent) showed much improvement; 4 improvement, and 9, slight or no improvement. The rate of recovery increases progressively from the hebephrenic to the catatonic to the paranoid group. The hebephrenic patient becomes more extroverted, interested and active; the catatonic patient loses his impulsiveness and negativism; the paranoid patient loses his intense interest in his delusions; he may or may not lose his hallucinations, but he certainly does not respond to them with the emotional impetus evident before operation. He does not answer the voices, does not fight back, does not try to keep the voices out by sticking his fingers in his ears. The outlook for the paranoid patients in general appears much more favorable than was anticipated.

One patient, with catatonia, failed to show improvement with the modified operation. After a four month period of observation, a second operation was performed, and all four quadrants were transected. This patient still shows no im-

TABLE 2.—*Results of Bilateral Prefrontal Lobotomy*

	Subcortical Transection of Lower Quadrants					Subcortical Transection of Upper and Lower Quadrants					
Disease	No. of Patients	Patients Much Improved	Patients Improved	Patients Slightly Improved	Patients Not Improved	No. of Patients	Patients Much Improved	Patients Improved	Patients Slightly Improved	Patients Not Improved	Total No. of Patients
Affective reaction types	3	2	1	..	..	..	..	..	..	..	3
Obsessive tension states	1	1	..	..	..	..	..	..	..	..	1
Psychoneuroses	1	1	..	..	..	1	1	..	..	..	2
Epilepsy with psychosis	2	1	..	1	..	2	..	..	2	..	4
Schizophrenias	15	6	4	3	2*	5	1	1	3	..	20
Total	22	11	5	4	2	8	2	1	5	..	30

* One patient had both types of operation.

TABLE 3.—*Results of Bilateral Prefrontal Lobotomy in Patients with Schizophrenia*

	Subcortical Transection of Lower Quadrants					Subcortical Transection of Upper and Lower Quadrants					
Type of Schizophrenia	No. of Patients	Patients Much Improved	Patients Improved	Patients Slightly Improved	Patients Not Improved	No. of Patients	Patients Much Improved	Patients Improved	Patients Slightly Improved	Patients Not Improved	Total No. of Patients
Hebephrenic	2	..	1	1	..	..	..	..	..	..	2
Catatonic	3	..	2	..	1*	1	1	..	..	..	4
Paranoid	8	4	1	2	1	3	..	..	3	..	11
Paranoid states	2	2	..	..	..	1	..	1	..	..	3
Total	15	6	4	3	2	5	1	1	3	..	20

* This patient had both types of operation.

provement, eight months after the second operation.

None of the patients became worse after the operation. No death occurred in our series either after operation or at a more remote period. There were no instances of infection. So far, in none of the patients has epilepsy developed. This sequela occurs, we believe, when the attack on the prefronal lobes is carried out through openings placed close to the premotor area; the resulting trauma, hemorrhage and edema which occur may more readily involve the motor regions and thus lead to the development of epileptic seizures. Our epileptic patients with psychosis exhibited no amelioration and no increase of the epileptic seizures after the lobotomy. Occasional transitory fluctuations in the blood pressure in either direction were noticed during the procedure, but no positive or permanent changes occurred.

Considerable thickening of the dura was a rather consistent observation for the patients with long-standing psychoses. In many patients a considerable collection of subarachnoid fluid was encountered and had to be evacuated. In some patients roentgenograms showed the injected iodized poppyseed oil intraventricularly; whether the negative pressure exerted by the suction caused a tear in the ventricle, or whether actual transection of the tip of the ventricle had taken place, is uncertain. Transection of the tip of the lateral ventricle in no way affected the therapeutic results.

Transitory incontinence occurred in 4 of the 22 patients in whom only the lower quadrants were sectioned and in 4 of 8 patients in whom all quadrants were transected. One patient had a dilated pupil on one side, which persisted for several days. Two patients had slight hemiparesis, which was minimal and rapidly disappeared. With 2 patients there was no speech production for about one week. Speech production was occasionally scanty and often in whispers, but it returned to its normal amount and intonation within a week. Some patients, however, exhibited transient slowing of speech, thought and motor activity; lack of interest, initiative and spontaneity, and flattening of facial expression. The retardation slowly disappeared, and the patient became more normal. These signs were less pronounced and returned to normal in a shorter period in patients in whom only the orbital quadrants were cut.

Delusional ideas might disappear rapidly or might continue with less emotional impetus than before. Auditory hallucinations might persist for some time but failed to keep the patient absorbed or upset. Postoperative confusion and disorientation were infrequently observed in patients, either with or without a favorable outcome. None of the patients was aware, or was willing to admit, that they had undergone an operation and showed no concern about it. Alertness and responsiveness on the first postoperative day did not interfere with the successful outcome of the operation. Improvement occurred gradually, within a few weeks, or might take as long as a year. Patience on the part of the physician was usually rewarded.

Most of the patients ate their meals heartily, some to excess. The gain in weight of the patients is indicated in table 4, and the results support the observations of Lyerly [13] and others. Frequently we noted an increase in tissue turgor and a fulness of facial features that made the patient appear younger.

During the period of convalescence the patient's psychotic behavior persisted to some extent; then inertia became more prominent, and the patient frequently complained of inability to overcome his dulness. The period of relative listlessness was followed by one of overactivity. It is at this time that the patient is most in need of assistance and direction toward a more normal adjustment. With anxiety diminished and the expression of the inherent trend reduced, a better integration of the personality can be established.

TABLE 4.—*Correlation of Changes in Weight with Clinical Results of Bilateral Prefrontal Lobotomy*

Clinical Change	Section of Orbital Areas	
	Gain in Weight	Loss of Weight
Much improvement	22	
Improvement	6	
Slight improvement	3	
No improvement	..	1

Study of the postparole status (table 5) reveals that at the time of writing 9 patients are keeping house and carrying the full burden of their responsibilities, 1 patient is partially employed, 3 patients are regularly employed, with 1 contributing to the manpower of the war, and another holds a position for the first time in her life. The operation apparently succeeds in salvaging considerable prepsychotic material which would have been irretrievably lost. The patients show resourcefulness, common sense, interest and planning for the future. Their lives are raised from an unsatisfactory level to one of useful activities. Their pathologic personality trends are now only faintly recognizable. The personality trends and the dynamics in the postoperative behavior are being carefully studied

13. Lyerly, J. G.: Prefrontal Lobotomy in Involutional Melancholia, J. Florida M. A. **25**:225, 1938.

and will be the basis of a future report, together with correlative psychologic testings.

COMMENT

The postoperative rate of recovery of 40 per cent of the total number of our patients compares favorably with the computed average of 31.3 per cent of seventeen other American centers. This also holds true for the recovery rates within the individual diagnostic groups.[14] The results of surgical intervention on only the orbital quadrants in these patients appear at least equal to the results obtained with transection of all four quadrants. The incidence of transitory postoperative urinary incontinence was found to be considerably lower (18 per cent) for the patients with the modified section of the orbital quadrants than for patients with section of all four quadrants (50 per cent).[10] In the postoperative course the dulling and slowing were less pronounced with the modified operation.

Freeman and Watts[10] (page 81) observed that placement of the cores in the lower part of the frontal lobes produced a higher incidence of good results than cores placed in the upper part of the frontal lobes. The significance of the orbital areas is apparent in the development of the surgical treatment of mental disorders. The various methods have progressed from the convexity of the prefrontal region to its subcortical strata, and finally to its orbital strata. The relation of emotional changes to lesions of the orbital area and the constancy of these lesions in 11 reported cases of changes in character, including the famous crowbar case of Harlow, were first pointed out by Welt[15] (1888). From a statistical study of 785 cases of cerebral tumors, Schuster[16] (1902) had the impression that involvement of the orbital lobes was to a higher degree responsible for the occurrence of emotional changes. The role of the orbital lobes in emotional changes becomes apparent from Berger's[17] work (1923). His material comprised chiefly bilateral prefrontal lesions (tumors, abscesses, injuries) within the brain substance or originating from the basal dura, such as tumors of the olfactory groove. He concluded that damage to the orbital lobes, especially to Brodmann's area 11, would without exception result in changes in personality.

From a study of vascular lesions of the brain, Alford[18] (1933) inferred that emotional disturbances were due to basal injuries. Kleist[19] (1937) attributed a central function in the emotional life to the orbital surface. Lemke[20] (1936) concurred in the opinion that changes in personality were particularly likely to appear in cases of tumor near the orbital surface. Grünthal[21] (1936) asserted that emotional disturbances and anomalies of behavior occur after trauma to the basal surfaces of the frontal lobes. In cases of Pick's disease he referred the initial lack of affective self control to damage to the orbital prefrontal area. Spatz[22] (1937) concluded that

TABLE 5.—*Status of Patients Following Bilateral Prefrontal Lobotomy (May 1942 to June 1944)*

	Subcortical Transection of Lower Quadrants					Subcortical Transection of Upper and Lower Quadrants					
Disease	No. of Patients	Patients Regularly Employed	Patients Partially Employed	Patients Able to Keep House	Patients Institutionalized	No. of Patients	Patients Regularly Employed	Patients Partially Employed	Patients Able to Keep House	Patients Institutionalized	Total No. of Patients
Affective reaction types	3	1	..	2	..	..	..	..	..	..	3
Obsessive tension states	1	..	..	1	..	..	..	..	..	..	1
Psychoneuroses	1	..	..	1	..	1	..	..	..	1	2
Epilepsy with psychosis	2	..	1	..	1	2	..	..	..	2	4
Schizophrenia	15	2	..	4	9	5	1	..	..	4	20
Total	22	3	1	8	10	8	1	..	..	7	30

14. Walker, A. E.: Psychosurgery: Collective Review, Internat. Abstr. Surg. **78**:1, 1944; in Surg., Gynec. & Obst., January 1944.

15. Welt, L.: Ueber Charakterveränderungen des Menschen infolge von Läsionen des Stirnhirns, Deutsches Arch. f. klin. Med. **42**:339, 1888.

16. Schuster, P.: Psychische Störungen bei Hirntumoren, Stuttgart, F. Enke, 1902.

17. Berger, H.: Klinische Beiträge zur Pathologie des Grosshirns: I. Herderkrankung der Präfrontalregion, Arch. f. Psychiat. **69**:1, 1923.

18. Alford, L. B.: Localization of Consciousness and Emotion, Am. J. Psychiat. **12**:789, 1933.

19. Kleist, K.: Bericht über die Gehirnpathologie in ihrer Bedeutung für Neurologie und Psychiatrie, Ztschr. f. d. ges. Neurol. u. Psychiat. **158**:159, 1937.

20. Lemke, R.: Ueber doppelseitige Hirntumoren, Arch. f. Psychiat. **106**:54, 1936.

21. Grünthal, E.: Ueber die Erkennung der traumatischen Hirnverletzung, Berlin, S. Karger, 1936, p. 76; Ueber ein Brüderpaar mit Pickscher Erkrankung, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:350, 1930.

22. Spatz, H.: Ueber die Bedeutung der basalen Rinde, Ztschr. f. d. ges. Neurol. u. Psychiat. **158**:208, 1937.

lesions of the "basal cortex," meningiomas, atrophy associated with Pick's disease, contusions and dementia paralytica lead to emotional changes and referred to the importance of the "basal cortex" for the functions of the "human psyche." In his recent detailed study on 32 cases of tumor, Rylander [23] (1939) obtained evidence that the basal parts of the frontal lobe play an important role in the emotional life, since 24 of his patients with parts of the orbital region removed showed emotional changes.

These results support the assumption that the basal parts of the frontal lobes are integrated in the emotional life. Further evidence for their role in the regulation of emotion comes from the experimental work on animals. Bilateral experimental lesions of the base of the brain (prechiasmal) in cats, according to Fulton and Ingraham [24] (1929), produced predominantly emotional disturbances. After prefrontal lobectomies, Walker [25] (1938) observed degeneration in the dorsal medial nucleus of the primate thalamus which he showed has not only connections with the hypothalamus but a projection system of fibers to the orbital surface of the frontal lobes (areas 9, 10 and 12).

All these observations point to a special significance of the basal part of the frontal lobes for the regulation of emotion (Goldstein [26]). The effect of section of the orbital part of the prefrontal lobes on the emotional life of patients with mental disease appears to confirm the assumption of an important role of the basal part of the prefrontal lobes in the emotional mechanism (Lashley [27]) of emotion.

23. Rylander, G.: Personality Changes After Operations on the Frontal Lobes, London, Oxford University Press, 1939, p. 296.

24. Fulton, J. F., and Ingraham, F. D.: Emotional Disturbances Following Experimental Lesion of the Base of the Brain (Pre-Chiasmal), J. Physiol. **67**:27, 1929.

25. Walker, A. E.: The Primate Thalamus, Chicago, University of Chicago Press, 1938.

SUMMARY

In a series of 22 patients with mental disorders, chiefly paranoid schizophrenia, a satisfactory therapeutic result was obtained with a modified technic of prefrontal lobotomy, in which only the orbital areas were sectioned.

The orbital areas of the frontal lobes seem to have a role in regulation of the emotions.

26. Goldstein, K.: The Mental Changes Due to Frontal Lobe Damage, J. Psychol. **17**:187, 1944.

27. Lashley, K. S.: Functional Determinants of Cerebral Localization, Arch. Neurol. & Psychiat. **38**: 371 (Aug.) 1937.

MENINGIOMA OBSTRUCTING THE FORAMEN MAGNUM

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OMAHA

Meningeal tumor obstructing the foramen magnum is relatively rare and until recently has seldom been diagnosed ante mortem. A survey of the literature up to 1937 reveals only 14 cases with adequate clinical records, in all of which the diagnosis was made at necropsy. In 1938 Cushing and Eisenhardt,[1] in their monograph, stated:

> Whether a meningioma arising from the basilar groove which must be overlain and concealed by a posteriorly dislodged medulla and its emerging nerves could be safely exposed and surgically enucleated must be left for further experience to determine.

They recorded 4 cases in which surgical treatment was attempted, in all of which the termination was fatal.

Since 1937 about 35 cases have been reported in which various kinds of tumors obstructing the foramen magnum were successfully removed. In at least two thirds of these cases the tumor was an upper cervical meningioma projecting into the foramen magnum or a supraforaminal tumor extending into the cervical space. The following authors made reports: Voss,[2] 4 cases; Gardner, Karnosh and McNerney,[3] 1 case; Fay,[4] 1 case; Lereboullet and Puech,[5] 2 cases; Ecker,[6] 1 case; Love and Adson,[7] 23 cases (all types of tumors); Friedman,[8] 2 cases; List,[9] 1 case (multiple meningioma).

In order to obtain unpublished cases of recovery, we questioned a number of neurosurgical clinics. Because of wartime difficulties many clinics were unable to review their records; the few responses showed a surprising number of cases of tumor involving the foramen magnum, as follows: the Lahey Clinic, 6 cases; the University of Michigan, 4 cases; the Jewish Hospital of Brooklyn, 7 cases; the Cleveland Clinic, 3 cases; the University of California, 2 cases, and the Temple University Clinic, 2 cases—a total of 24 cases with recovery. In addition, a number of fatal cases were reported. These figures show that tumor involving the region described is not so rare as a review of the literature indicates and that since Cushing's pessimistic observation in 1938 neurosurgical technic has been greatly improved.

Our study was prompted by a recent unusual case of meningioma of the basilar groove occurring in a critically ill patient who for several months presented serious problems of clinical management. Difficulties in the diagnosis of this syndrome involve the differentiation of a large number of conditions, such as amyotrophic lateral sclerosis, syringomyelia, combined sclerosis (dorsolateral spinal degeneration), neuronitis, bony deformities of the foramen magnum, atlas and axis (platybasia) and congenital myelodysplasia.

REFORT OF A CASE

History.—C. H., a flying instructor in the Army aged 23, had a past history of no importance except for an attack of "flu" a year before when he was at a camp in Texas. He was treated with sulfonamide compounds, was in bed a week, and lost 10 pounds (4.5 Kg.) in weight. He had severe occipital headaches but no pain

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1. Cushing, H., and Eisenhardt, L.: Meningiomas, Springfield, Ill., Charles C Thomas, Publisher, 1938, pp. 87-91 and 169-180.

2. Voss, O.: Basale Meningeome der hinteren Schädelgrube, Arch. f. klin. Chir. **189**:494-497, 1937.

3. Gardner, W. J.; Karnosh, L. J., and McNerney, J. C.: Meningeal Tumor in the Foramen Magnum, Arch. Neurol. & Psychiat. **39**:1302-1307 (June) 1938.

4. Fay, T.: Localization and Treatment of Lesions of the Spinal Cord, S. Clin. North America **18**:1577-1597, 1938.

5. Lereboullet, J., and Puech, P.: Tumeur de la moelle cervicale haute avec prolongement intracranien simulant la sclérose latérale amyotrophique. opération. Guérison, Bull. et mém. Soc. méd. d. hôp. de Paris **56**: 828-830, 1941.

6. Ecker, A. D.: Removal of Tumor Arising Anterior to the Medulla, Arch. Neurol. & Psychiat. **46**:908-912 (Nov.) 1941.

7. Love, J. G., and Adson, A. W.: Tumor of the Foramen Magnum, Tr. Am. Neurol. A. **67**:78-81, 1941.

8. Friedman, E. D.: Compression of the Upper Cervical Cord in the Guide of Combined System Disease, Internat. Clin. **3**:102-110, 1941.

9. List, C. F.: Multiple Meningiomas: Removal of Four Tumors from the Region of the Foramen Magnum and Upper Cervical Region of the Cord, Arch. Neurol. & Psychiat. **50**:335-341 (Sept.) 1943.

in the head or neck thereafter. He was still weak on return to work.

Six months later, in October 1942, he again lost appetite and weight, but thought that he was neurotic because of emotional strain and worry over several accidents among cadet students. He noted a tight, bandlike sensation about the abdomen and difficulty at times in starting urination.

In February 1943 he noticed progressive numbness and weakness of the left hand, felt too weak to ride his bicycle to work and had increasing difficulty in getting in and out of the airplane. His fingers became so numb that he could not button his clothes. The last day he flew (two weeks before our examination) he got out of the plane only after a great struggle, wheeled his bicycle home and collapsed on the lawn, the bicycle falling on top of him.

He was sent by plane from Texas to his home in Omaha on two weeks' leave. Tremor of the right hand then developed, with inability to write or feed himself; weakness of the legs and spasmodic involuntary jerking movements occurred, and breathing became very difficult.

Neurologic Examination.—There were paralysis of the left side of the tongue, with atrophy and fibrillations, and notable paresis of the neck muscles and the intercostal and diaphragmatic muscles. The patient was extremely dyspneic, using the accessory muscles of respiration. Examination showed spastic flexor paralysis with atrophy of both arms, which was most conspicuous in the muscles of the hand; fibrillation of the muscles of the shoulders; exaggerated tendon reflexes, and a Hoffmann reflex bilaterally. The abdominal and cremasteric reflexes were absent. The legs showed almost complete spastic paralysis, with exaggerated tendon reflexes, clonus and all the reflexes indicative of involvement of the pyramidal tract. The slightest stimulation produced extreme massive involuntary spasm. The results of sensory examination were hard to evaluate because of the patient's difficulty in breathing and talking. Hypalgesia of the left arm and the left side of the trunk was patchy and questionable. There was no spontaneous pain and no involvement of proprioceptive function.

Course of Illness and Further Studies.—The patient was immediately hospitalized, on April 5, 1943, with a working diagnosis of acute amyotropic lateral sclerosis, which was later ruled out by the results of the first examination of the spinal fluid, with its total protein content of 500 mg. per hundred cubic centimeters. Because of impending complete respiratory paralysis, the patient was placed in a respirator, where he remained almost continuously for three months.

For about sixty days further neurologic examination was difficult, since the patient could remain out of the respirator only a few minutes at a time. During April 1943 the motor paralysis remained about the same—spastic quadriplegia with little voluntary movement, chiefly a slight movement of the fingers and toes; conspicuous fibrillations, which were readily seen, and severe emaciation, the weight being probably about 110 pounds (49.9 Kg.). Definite sensory changes had appeared in the form of bilateral loss of pain sensation throughout the lower cervical and all the dorsal and lumbar segments. The sacral segments were not involved; touch sensation was well preserved. The patient overreacted to painful stimuli, describing them as a burning sensation (similar to the thalamic reaction).

In May weakness of the sternocleidomastoid and trapezius muscles with atrophy was noted on the left side. Severe spasmodic involuntary jerking movements of the lower extremities occurred frequently; but the intercostal muscles seemed to regain power, and the patient could remain out of the respirator for longer periods.

Routine examination of the blood and urine revealed nothing abnormal. Roentgenograms of the skull and the cervical portion of the spine showed normal structures. In addition to the sensory paralysis earlier described, the cervical segments as high as the second became affected. Vibration sensibility, position sense and astereognosis were impaired in the upper extremities. As noted, first examination of the spinal fluid showed a total protein content of 500 mg. per hundred cubic centimeters. A second examination, in May, revealed a pressure of 150 mm. of water, normal hydrodynamics and a total protein content of 250 mg. per hundred cubic centimeters. Cisternal puncture, twice attempted, yielded no fluid, and the unnatural resistance encountered suggested obstruction at the foramen magnum. A third spinal puncture, on June 10, revealed 170 mm. of water. On careful jugular compression, the pressure rose to 230 mm. and did not fall back to the initial reading; the fluid was slightly xanthochromic.

The impression at this time was that of a lesion involving the left side of the medulla, localized by the eleventh and twelfth cranial nerves and causing obstruction of the foramen magnum—either a tumor associated with syringomelia or an extramedullary growth. After neurosurgical consultation it was decided to defer operation because of respiratory embarrassment, but a course of high voltage roentgen ray treatments was begun. Slow improvement in respiratory function followed, and gradually the patient was able to get along without the respirator.

The patient was then sent home for thirty days, and forced nutritional measures were continued. Neurologic examinations revealed the same spastic quadriplegia, with atrophy and fibrillations. At times spasmodic movements of the neck occurred. A fourth examination of the spinal fluid showed evidence of complete spinal block.

Surgical Procedures.—The patient was returned to the hospital on Sept. 4, 1943, for a two stage operation. In the first operation, on September 6, Dr. J. Jay Keegan performed a suboccipital decompression with local anesthesia. The medulla was observed to be elevated, flattened and displaced to the right by a firm extramedullary tumor, presenting in the left side of the foramen magnum. A small piece removed for biopsy showed a typical meningioma (figure). Because of respiratory embarrassment removal was not attempted.

For a few days there were symptoms of meningeal irritation from blood in the spinal fluid, but the patient showed rapid improvement, especially in respiration. Motor and sensory paralysis improved within one month, so much that the patient could walk unassisted. By November functional recovery was almost complete; only the motor paralysis of the left eleventh and twelfth cranial nerves remained.

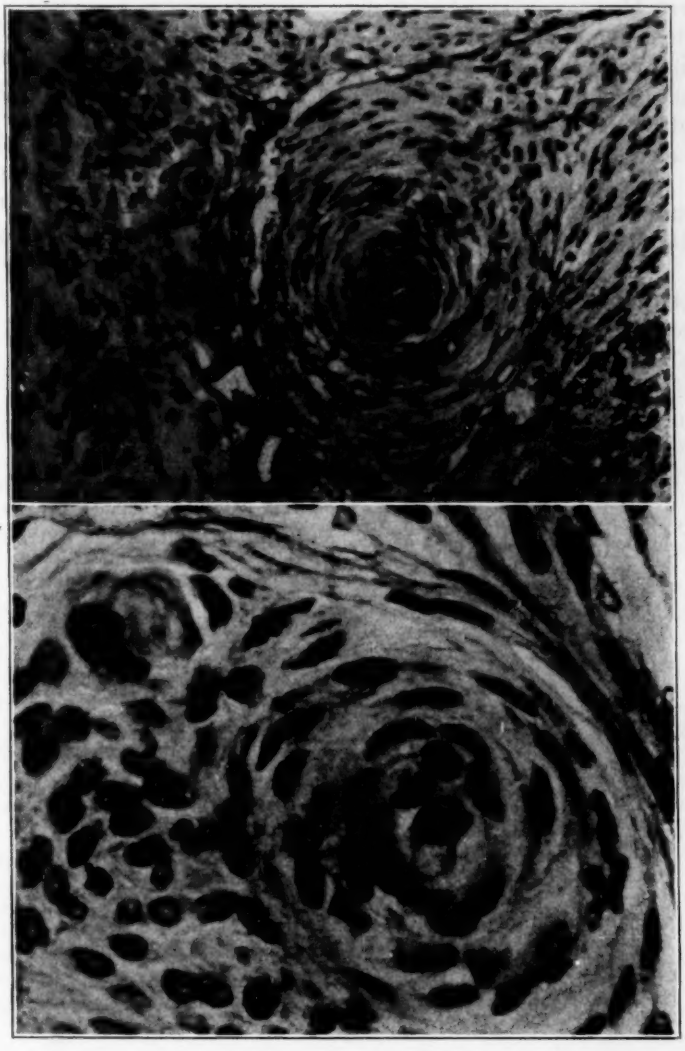
On November 15, at a second operation, a firm, nodular tumor was exposed in the foramen magnum, the main portion lying above the basilar groove, beneath the medulla, and a smaller portion projecting through the foramen magnum about 1 cm. into the spinal canal. Careful dissection completely freed the lower portion, but removal necessitated the sacrifice of some of the roots of the eleventh cranial nerve. Dissection was then extended around the upper, and larger, portion of the tumor, which was separated with

difficulty from the cerebellum and the basilar groove, to which it was firmly adherent and where it apparently had its origin. The firm, fibrous tumor was removed piecemeal, the total weight being 8 Gm. When dissection was completed, the flattened medulla and the left eleventh cranial nerve were quite free. The twelfth cranial nerve was not seen, and it was thought that it had been sacrificed during removal of the portion near the condyloid foramen.

parently, neither the eleventh nor the twelfth nerve was completely sacrificed at operation. The patient returned to full duty as an air pilot instructor in May 1944.

COMMENT

A review of symptoms and signs reported by the various authors shows no clearcut clinical



The tumor is composed of spindle-shaped cells, showing a conspicuous tendency to formation of whorls. Some areas were fibrotic, and psammoma bodies were present.

A diagnosis of meningioma of the left condyloid foramen compressing the medulla at the foramen magnum was thus established.

The patient recovered uneventfully and left the hospital in two weeks. He then went to Florida for the winter, rapidly gained weight up to 150 pounds (68 Kg.) and through swimming exercise became very muscular. Neurologic examination six months after removal of the tumor showed no abnormal signs except for slight atrophy of the posterior left half of the tongue and slight weakness of the left trapezius muscle. Ap-

syndrome for tumors in this location. Many patients, like ours, had no pain; quadriplegia, with both motor and sensory disturbance, was consistently present. Because of the rather large space of the cisterna magna the tumor may grow to considerable size before signs of block appear. Roentgenographic evidence is usually negative for tumor in this region but does exclude platybasia; intraspinal myelographic study may be

necessary. There is little consistency in the neurologic signs. Although in all cases spastic signs were present bilaterally, sensory signs were seldom, if ever, present, the condition thus simulating amyotrophic lateral sclerosis. In other cases conspicuous signs referable to the posterior columns pointed to combined system disease; in still other cases sensory dissociation of syringomyelic type was present. Astereognosis and cerebellar signs were likewise reported.

The most consistent symptoms and signs are attacks of suboccipital pain, followed by bilateral spastic paralysis and some form of sensory paralysis, with unilateral palsies of the lower cranial nerves and an increased protein content of the spinal fluid. If signs of block are present, the diagnosis is certain. In a few instances evidence of increased intracranial pressure was also noted.

Since studies of the spinal fluid are absolutely necessary for correct diagnosis, it is important to note that in many fatal cases reported the patient died within a few hours after spinal puncture. One of us (A. E. B.)[10] has described elsewhere the problem of cerebellar herniation and the hazards of lumbar puncture in cases in which diagnostic signs of obstruction of the foramen magnum appear. The danger of sudden respiratory paralysis from tumor in this region is ever present, and the difficulties in managing this complication are well illustrated by our case. This danger forced us to use a respirator for several months, a life-saving procedure in our opinion.

10. Bennett, A. E.: Cerebellar Herniation into Foramen Magnum, J. A. M. A. **100**:1922-1925 (June 17) 1933.

CONCLUSIONS

Up to 1937 no case of operative recovery from meningioma obstructing the foramen magnum had been reported. Our compilation of about 60 reported and unreported cases of recovery since that time shows that this tumor is not infrequent and that notable advance in neurosurgical management has occurred.

In a case of meningioma of the condyloid foramen reported here respiratory paralysis required management in a respirator for three months. Complete recovery followed a two stage operation.

The diagnosis of neoplastic lesions in this location is particularly difficult because the symptoms resemble those of many other disorders and there is no clearcut clinical syndrome. Study of the spinal fluid is a necessary part of the diagnosis, but spinal puncture is extremely dangerous.

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DIVERGENCE PARALYSIS AND HEAD TRAUMA

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We have been able to find the report of only 5 cases of divergence paralysis as a complication of head injury. Bielschowsky [1] recorded the case of a youth aged 17 who sustained a cerebral concussion six weeks before ophthalmologic examination. He began to see double at a distance a few days after the accident. Four weeks after he was first seen there was no alteration in his condition. Weed [1b] reported 4 cases, in 1 of which the paralysis persisted three years. In a series of 1,550 cases of head injury encountered in private practice, we found 6 cases of divergence paralysis. In view of the paucity of such reports, a brief summary of these cases may be of clinical value.

REPORT OF CASES

CASE 1.—A girl aged 11 years complained of headache, double vision and difficulty in reading which had followed an accident two years before. She had fallen when pushed, striking the back of her head. She was not unconscious at that time but spoke irrationally for a short period. She vomited after the accident, was confused and showed mental changes for several hours. She had frontal headaches, which became intensified with ocular and physical effort, was nervous and found it difficult to read because of ready ocular fatigue. Glasses did not improve her vision. Examination revealed divergence paresis; the ankle jerks could not be elicited even with reenforcement; the left knee jerk was more active than the right, and the abdominal reflexes were all readily exhaustible.

CASE 2.—A white woman aged 28 struck the back of her head on falling when a table slipped. She was unconscious for a short, but undetermined, period, vomited and began to see double soon after the accident. The double vision persisted up to the time of examination, eight days later. There was occasional convergence of the eyeballs. She also complained of paroxysmal pains in the back of the head and dizziness on attempting to sit up. Five days later she had a convulsive seizure. There were involuntary movements of the head from side to side, repeated chewing movements and occasional incoherent spontaneous utterances. No convulsive movements were reported. She recalled nothing after the spell cleared.

Her previous history included poliomyelitis at the age of 2 years, followed by paralysis from the waist down. She was still disabled but walked with the aid of crutches. There was no history of double vision prior to the accident.

Examination showed occasional spasms of convergence. Between such spasms the red glass test revealed a divergence defect in the nature of homonymous diplopia in the central field; the distance between the images became greater as the source of light was moved away from the eyes. There was no evidence of palsy of the abducens nerve. Residual signs of old poliomyelitis were prominent, with atrophy and severe impairment of movement in the lower limbs and absence of reflexes. The patient complained of dizziness with passive movements of the head.

CASE 3.—A man aged 45 complained of having had headaches, dizziness, nervousness and double vision since an accident two years before, in which he was hit on the head by a steel hoisting cable and was thrown to the ground, striking his head. There was bleeding from the scalp and face. He was unconscious for fifteen minutes and vomited. He was hospitalized for three weeks. After leaving the hospital, he complained of recurring sharp pain in the back of the head every few hours, especially with bending and on attempting to read. The dizziness improved somewhat shortly after the accident. He had had ringing in both ears on and off since the injury. Double vision was noted immediately after the accident, especially on his looking at distant objects. He was irritable, with pronounced intolerance to noise. He became nauseated occasionally on bending. A month after he left the hospital, while sitting, he suddenly lost consciousness. Clonic movements were noted in the left upper extremity. He vomited after this seizure.

Examination showed that the blood pressure was 140 systolic and 74 diastolic and the pulse rate 72. There was a 3/8 inch (0.9 cm.) scar in the right parietal region and another scar, measuring 3/4 inch (1.9 cm.), below it. Auditory acuity was diminished on the left, with lateralization of the Weber sign to the left. The right pupil was slightly irregular and larger than the left; both reacted sluggishly to light and somewhat better in accommodation. The left palpebral fissure was the narrower. There was definite evidence of divergence paralysis. Studies showed concentric contraction of both fields. There was generalized hyperreflexia. The patient had amnesia for the accident and for a short period afterward. He was impatient and irritable.

CASE 4.—A man aged 41 six years previously was hit on the right ear while driving and was thrown out of the car. He was unconscious for an hour. A vertical linear fracture in the postparietal region just above the left mastoid was demonstrated roentgenographically. The patient complained of headaches, spells of dizziness and double vision, all dating from the accident.

Examination revealed divergence paralysis.

CASE 5.—A man aged 47 was driving a car when it collided with another. He was unconscious for ten minutes and remained in bed for six weeks. He complained of dizziness on bending his head. Double vision for distance had been present since the accident.

Examination three years after the trauma disclosed nerve deafness on the right side. A divergence defect was demonstrated with the red glass test.

1. Bielschowsky, A.: Ueber die sogenannte Divergenzlähmung, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **28**:110, 1900.

1a. Weed, H. M.: Divergence Paralysis Due to Head Injury, Tr. Am. Acad. Ophth. **39**:189, 1934.

CASE 6.—A white woman aged 42 was struck on the head by a heavy valise which fell from a rack. She was unconscious for a short, but undetermined, period. There was bleeding from the nose; her face and right eyelid were swollen, and she vomited. She saw double for three weeks after the accident and still had diplopia occasionally.

The red glass test made fifteen months after the trauma disclosed homonymous diplopia in the central field; a hemisensory functional syndrome was also present on the right.

COMMENT

A review of 17,783 cases of acute and chronic head injuries reported in the literature from 1906 to 1943 [2] revealed no instances of divergence paralysis with the exception of the cases of Bielschowsky and Weed. Somberg [3] stated that no cases of divergence paralysis had been seen after head injury. Several authors indicated that diplopia was present but gave no explanation for it (Wortis and Kennedy [2r]). The absence of reports of divergence paralysis as a complication of head injury is possibly due to the fact that the patient is often too ill, especially in the acute stage, to be tested and, also, to the failure of the physician to make careful examinations to determine its presence. Aubineau [2a'] referred to 2 cases of disorders of associated movements of the eyes following head trauma but gave no details.

The question of the probable functional or hysterical nature of divergence paralysis has been discussed by von Hippel [2o'] and Clarke.[4] In our opinion, there is insufficient proof that this condition can occur on a hysterical basis. The appearance of divergence palsy after a psychic trau-

2. (*a*) Crandon, L. R. G., and Wilson, L. T.: Fracture of Base of Skull—530 Cases, Ann. Surg. **44**:823, 1906. (*b*) Besley, F. A.: A Contribution to the Subject of Skull Fractures: Analysis of One Thousand Cases and Report of Seventy-Four Cases Examined at Necropsy, J. A. M. A. **66**:345 (Jan. 29) 1916. (*c*) Sharpe, W.: Observations on the Diagnosis and Treatment of Brain Injuries in Adults, ibid. **66**:1536 (May 13) 1916. (*d*) Mixter, W. J.: Fractures of the Base of the Skull at Massachusetts General Hospital, Boston M. & S. J. **177**:518, 1917. (*e*) Wilensky, A. O.: Fracture of the Skull with Special Reference to Its Neurological Manifestations, Ann. Surg. **70**:404, 1919. (*f*) Stewart, J. W.: Fractures of the Skull, J. A. M. A. **77**:2030 (Dec. 24) 1921. (*g*) Moorhead, J. J., and Weller, W.: Fractures of the Skull in Children, Ann. Surg. **74**:72, 1921. (*h*) Kearney, J. 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3. Somberg, J. S.: Ocular Defects Arising from Skull Injuries, Bulletin 10, New York State Bureau of Workmen's Compensation, Medical Division, Albany, 1924.

4. Clarke, C. P.: Paralysis of Divergence of Functional Origin, Am. J. Ophth. **19**:789, 1936.

ma does not prove its functional nature. Among over 2,000 cases of psychoneuroses observed in private practice, no case of divergence paralysis was encountered which could be considered entirely functional. In this material were represented many other functional ocular disturbances, such as amaurosis, tubular fields, ptosis, blepharospasm, monocular diplopia and convergence and accommodation spasm. There is no evidence that divergence palsy responds to forceful suggestive therapy or hypnosis. The association of functional sensory changes and other conversion phenomena does not prove the hysterical nature of the paralysis.

The presence of convergence spasm in case 2 raises the question whether divergence paralysis is really due to convergence spasm. The persistence of the homonymous diplopia for years, as in case 3, is somewhat against the theory of the existence of spasm. It is reasonable, also, to expect an insufficiency of convergence if spasm of this type is present. There was no evidence of such a defect of convergence in any of the patients examined.

We are of the opinion that in such cases the head trauma causes injury to the hypothetic center for divergence in the midbrain (Bender and Savitsky [2b']). In view of the persistence of the complaint in some of our cases (as long as five years after the injury), the lesion is occasionally irreversible, perhaps a laceration.

SUMMARY AND CONCLUSIONS

Six cases of divergence paralysis as a complication of head injury were encountered in a series of 1,550 personally observed cases of head trauma.

Only 5 similar cases were found among 17,783 cases of head injury reviewed in the literature.

We believe this syndrome is more common than has heretofore been indicated.

1882 Grand Concourse.

ELECTROENCEPHALOGRAPHIC EVALUATION OF PRIMARY BEHAVIOR DISORDERS IN CHILDREN

CORRELATIONS WITH AGE, SEX, FAMILY HISTORY AND ANTECEDENT ILLNESS OR INJURY

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In a number of reports it has been shown that there is a significant preponderance of the "too slow" type of electroencephalogram for children with disturbances diagnosed as primary behavior disorders. Jasper, Solomon and Bradley,[1] the first to report this observation, discovered that of a sample of 71 children, 73 per cent showed slow abnormalities. The finding has been repeatedly confirmed by a large number of investigators.[2] From this observation it appears that when a relatively new yardstick, the electroencephalogram, is applied, two forms of the disturbance appear: primary behavior disorders associated with a normal electroencephalogram, and primary behavior disorders associated with an abnormal electroencephalogram, the number of children with the latter at least equaling, and probably exceeding, the number with the former.

Records which are of the "too slow" type are frequently associated with epilepsy and are broadly related to psychomotor seizures.[3] It can be argued that the so-called primary behavior disorders with an abnormal electroencephalogram are in reality a hitherto undetected form of behavior disorder associated with epilepsy, or perhaps a variant of psychomotor epilepsy. In addition, it has been discovered that there are strong hereditary characteristics in the electroencephalograms of epileptic persons, a great proportion of the seizure-free parents of epileptic children exhibiting abnormal waves and, conversely, the seizure-free children of epileptic parents showing a considerable amount of abnormal electrocortical activity.[4]

Furthermore, head injury is known to result in abnormality of the electroencephalogram, as are also anoxia, encephalitis and other conditions leading to known cortical involvement,[3] independent of epilepsy. Consequently, it can be argued that any of these conditions might be associated with primary behavior disorders with abnormal electroencephalograms.

Since it cannot be told from the electroencephalogram, except in a restricted number of cases, whether the abnormality has its origin in genetic factors or in traumatic or infectious

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cerebral injury, recourse to the history of the patient and of the patient's relatives is required to evaluate the etiologic factors in the record.

The present study is an extension of the previously reported observations and implications.

METHOD

Of a group of children with psychiatric disorders from whom electroencephalograms had been obtained, the conditions of 67 were diagnosed as primary behavior disorders. A definition of primary behavior disorders in children has never been adequately formulated. Kanner [5] pointed this out in his discussion of the problem of nosology for children when he stated:

"The manifoldness and complexity of behavior disorders have made systematic grouping extremely difficult. . . . This is especially true of children because personality is still in *statu nascendi* and any cataloging, therefore, can at best be anticipatory rather than conclusive." Yet of the all-inclusive group of behavior disorders in children, certain categories can be delimited in descriptive or etiologic terms, implying thereby laws which allow prediction. Among various outlines for the psychiatric classification of problem children is that of Brown, Pollock, Potter and Cohen,[6] which incorporates a combination of etiologic and descriptive nosology. Their principal groups are (1) mental deficiencies; (2) psychoses; (3) psychoneuroses and neuroses; (4) convulsive disorders, including epilepsy; (5) behavior disorders with somatic disease or defect; (6) psychopathic personalities; (7) educational disabilities; (8) primary behavior disorders; (9) social problems, and (10) other problems. We follow their nosology, so that our definition of primary behavior disorders coincides with theirs except that we incorporate their group of psychopathic personalities in our definition. This occurs because we are unable to differentiate these two groups on either a descriptive or an etiologic basis. Primary behavior disorders cannot be thought of as constituting a specific entity but are to be regarded as a heterogeneous collection of disorders formed as a result of the exclusion of other, better described, groups.

Criteria for inclusion of cases in the present study were a composite record of the psychiatric, physical, neurologic, laboratory and psychometric examinations and a detailed social history. The social histories were comprehensive and were obtained primarily from one or both parents; in a few cases they were obtained from a person, other than the parents, who accompanied the child to the clinic. In most instances this material was supplemented or corroborated by social agencies, physicians, teachers, friends or other nonfamily members. No case was included in which the symptoms were suspected of being sequelae of a physical illness or injury.

From these collected data it was then possible to investigate the relation of the electroencephalogram to factors of age, sex, family history and antecedent injury or severe illness.

The group included children of both sexes and ranged in age from 6 through 15 years. All the children had intelligence quotients above 80 on the revised form of the Stanford-Binet intelligence test. Physical examination of these 67 children at the time they were studied indicated no recognized relation to the behavioral problems presented. The most common and frequent findings were carious teeth, malnutrition, underdevelopment, enlarged tonsils, acne, visual refractive errors and obesity. One child had chronic bronchitis. In another youngster rheumatic fever with cardiac involvement developed while he was being treated in the hospital (but after our examinations), and he was transferred to the pediatric ward. Another child had bilateral deafness.

From the detailed history obtained for each child certain data were selected and used as criteria for the designation of the family history as positive or negative. Preliminary examination of the histories revealed four ancestral types which could be clearly defined and labeled as positive, on the basis of the presence of one of the following disorders: (1) psychosis, (2) maladjusted personality (this was sometimes difficult to determine, but a positive decision was made if the person involved had reputedly never been able to make an adjustment because of inability to control his emotional responses, and hence was in repeated difficulties), (3) chronic alcoholism (this was selected because of the relative rarity of this condition in this section of the country [Iowa], and its almost constant association with severe personality maladjustment) and (4) epilepsy. In most instances a positive history included the occurrence of the condition in a parent or grandparent, the history only rarely being called positive on the basis of the involvement of a collateral line.

The antecedent illnesses and injuries which were selected for consideration were (1) prematurity, (2) birth injury or questionable birth injury, (3) head injury complicated by unconsciousness, (4) severe illness complicated by delirium, (5) convulsions in infancy (a single, isolated convulsion not believed to be of epileptic origin) and (6) a period of anoxemia, either at birth or later in life.

Six lead electroencephalograms were made for virtually all subjects (in rare cases three lead records were obtained), monopolar recordings being made from the left and right occipital, motor and frontal regions of the skull. Records were made with the subject relaxed and the eyes closed. Small lead pellets, secured to the end of a fine enamel-insulated wire, were cemented to the scalp with collodion, an electrode jelly of the electrocardiograph type being used to enhance conductivity. A three channel, ink-writing oscillograph recorded the electroencephalogram. All recordings were at least eighteen minutes in length.

In analysis of the electroencephalographic records a subjective classification was employed, since no absolutely quantitative norms are as yet available for children. A preliminary inspection of all of the records indicated that it would be possible to place each record into one of a series of categories. The entire series of records was then reviewed and assigned, on the basis of experience in obtaining records from 270 unscreened normal children (by one of us, J. R. K.), to its appropriate class. The most thorough quantitative data on what constitutes the normal electroencephalogram in children have been published by Lindsley,[7]

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6. Brown, S.; Pollock, H. M.; Potter, H. W., and Cohen, D. W.: Outline for the Psychiatric Classification of Problem Children, Utica, N. Y., State Hospital Press, 1937.

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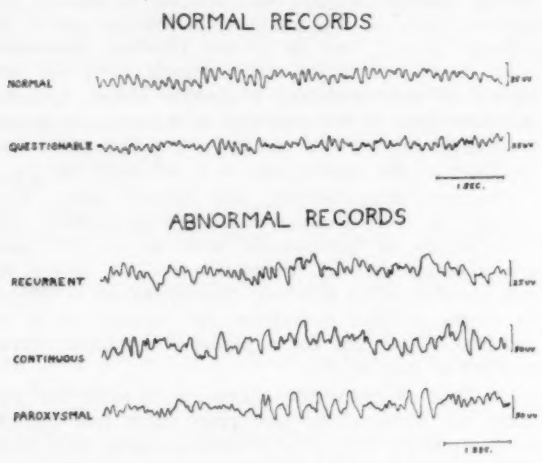
who determined the variation of frequency limits with age. These limits were used to define an electroencephalogram as "normal." Gibbs and Gibbs [8] published an essentially qualitative chart of the relative incidences of slower than dominant frequencies in the electroencephalogram at various ages. This chart and the experience of one of us (J. R. K.) were used to classify a record as other than normal.

The exact classification is, of course, essentially subjective. Definitions of the categories follow.

1. Normal: Records within the normal frequency limits derived from Lindsley's age frequency table.

2. Questionably normal: Records presenting not only the dominant frequency for the age expected, but either too slow or too fast frequencies nondominant, but present to a sufficient extent to make difficult the qualitative estimate of a normal record. (Such records are not included in the final statistical treatment of these data because of their uncertain allocation; clinically we consider these electroencephalograms "normal" in order to be conservative.)

3. Abnormal: Records presenting dominant frequencies above or below the age norm. These frequencies



Sample strips of electroencephalograms, illustrating the characteristic features of the record in each electroencephalographic category. At the left of each strip is the name of the category as defined in the text. At the right is the calibration for microvolts and for one second.

These sample strips were all obtained from patients 8 years of age. For different ages the normal frequencies vary, being slower for the younger and faster for the older children, but the relative differences among the categories remain the same.

may appear (*a*) recurrently, in long bursts of several seconds; (*b*) continuously, with no normal frequencies present, or (*c*) paroxysmally, as a sudden change to a seizure-like pattern, but usually occurring against a dominant background of normal activity; it could, and sometimes did, occur against a continuously too slow background, when the record was classified as "paroxysmally abnormal."

The figure presents samples of records illustrating each category. This classification was applied only to the "resting" record. No record obtained during or after hyperventilation was used in this study.

DATA

The electroencephalograms for the 67 patients were classified as follows:

Normal	27	(40 per cent)
Questionably normal	7	(10 per cent)
Recurrently abnormal	18	(27 per cent)
Continuously abnormal	8	(12 per cent)
Paroxysmally abnormal	7	(10 per cent)

If the last three categories are combined, 33 patients (49 per cent of the series) had abnormal records. Hereafter this combined group will be considered as a unit. This percentage is slightly lower than, but consistent with, the percentage reported by other investigators [8] for children with primary behavior disorders and is considered higher than the percentage to be expected from a group of unscreened but presumably normal children.[9] The fact that our percentage of abnormal records for the entire series is lower than that reported by other authors may be attributed to our attempt to exclude all known or probable conditions of organic origin at the outset.

TABLE 1.—*Analysis of the Electroencephalogram in Relation to Age and Sex*

	Encephalograms						
	Males			Females			
Age	Abnormal	Questionably Normal	Normal	Abnormal	Questionably Normal	Normal	Totals
6	1	..	1	..	..	..	2
7	..	..	1	..	..	1	2
8	3	2	3	1	..	..	9
9	..	1	1	..	..	1	3
10	..	..	3	1	..	..	4
11	1	..	1	2	..	..	4
12	3	1	2	1	..	..	7
13	8	1	..	..	..	..	9
14	4	..	5	1	1	3	14
15	4	1	5	3	..	..	13
Totals	24 (46%)	6 (12%)	22 (42%)	9 (60%)	1 (7%)	5 (33%)	67

Table 1 presents an analysis of the electroencephalograms in relation to age and sex. The distribution for age shows a greater percentage in the upper levels, for 36 (54 per cent) of the patients were in the age groups of 13, 14 and 15 years. There is an apparent difference in the percentage of abnormal electroencephalograms

8. Jasper, Solomon and Bradley.[1] Lindsley and others.[2]

9. In a personal communication Mr. C. E. Henry, who has over 2,000 electroencephalographic records on an unscreened group of children, stated that the percentage of abnormal records, with essentially the same classification, was approximately one-half ours. For a group of 270 unscreened children, records on whom were made by one of us (J. R. K.), this percentage was approximately one-quarter the value for the group considered in the present report.

between the younger and the older age groups. Statistically, however, the difference in the distribution of the types of electroencephalograms of patients younger and of patients older than 12 years of age is not significant at the 5 per cent level, and one need not reject the hypothesis that the two distributions are the same. Other investigators [2] have reported that there is a greater incidence of abnormalities in younger than in older patients. This is at variance with the tendencies of our data, even though these tendencies are themselves insignificant. Perhaps the explanation lies in the judgments of normality employed in the various investigations, for at earlier ages there is normally frequent slow activity.

Fifty-two (77 per cent) of the patients were males, a ratio of 3:1. There were no statistically significant differences in regard to the distribution of abnormal or normal electroencephalograms for the two sexes. Thus, the data

TABLE 2.—*Analysis of the Electroencephalogram in Relation to Family History and Antecedent Severe Illness or Head Injury*

	Electroencephalograms		
		Questionably	
	Abnormal	Normal	Normal
Family history only	9 (48%)	5 (26%)	5 (26%)
Illness or injury only	7 (54%)	.....	6 (46%)
Family history and illness or injury	13 (65%)	1 (5%)	6 (30%)
No positive family history or previous illness or injury	4 (27%)	1 (6%)	10 (67%)
Totals	33 (49%)	7 (11%)	27 (40%)

in this table indicate that age and sex are not significant factors in relation to the electroencephalographic characteristics observed.

Table 2 presents an analyses of the electroencephalograms in relation to antecedent illness, injury and/or family history. Thirty-nine patients (58 per cent) had a positive family history, and 33 (49 per cent) had a positive history of illness or injury. The striking feature in this table is the difference between the patients who had neither a positive family history nor any significant antecedent illness or injury and the patients who had both a positive family history and a history of illness or injury. Of the former group, 4 patients (27 per cent) had abnormal electroencephalograms, in contrast to 13 patients (65 per cent) of the latter group. Although the absolute number of patients is small in each group, it was possible to subject the two distributions to a statistical treatment to discover whether they differed significantly. With the method of χ^2, a level of significance of 3 per cent was obtained. This means that the difference could be attributed to chance in only 3 out of 100 experiments and is thus statistically significant.

Further examination of this table indicates that 9 patients (48 per cent) had abnormal electroencephalograms in the group with a positive family history only and 7 (54 per cent) in the group with a history of antecedent illness or injury alone. When the distributions for the group with a positive family history and the group with neither a positive family history nor a history of illness or injury were compared by the χ^2 test, the difference was found to be significant between the 5 and 10 per cent levels of confidence. When the distributions for the group with antecedent illness or injury and the group with neither a positive family history nor antecedent

TABLE 3.—*Analysis of the Electroencephalogram in Relation to Positive Family History*

	Electroencephalograms		
		Questionably	
Family History	Abnormal	Normal	Normal
Psychosis only	2	1	2
Psychosis and maladjusted personality	1	3	1
Psychosis and alcoholism	1	..	..
Psychosis and epilepsy	1	1	..
Totals	5	5	3
Maladjusted personality	9	1	3
Maladjusted personality and psychosis	1	3	1
Maladjusted personality and alcoholism	1	..	2
Maladjusted personality and epilepsy	1	..	..
Totals	12	4	6
Alcoholism	3	..	2
Alcoholism and psychosis	1	..	..
Alcoholism and maladjusted personality	1	..	2
Alcoholism and epilepsy	1	..	..
Totals	6	..	4
Epilepsy	2	..	1
Epilepsy and psychosis	1	1	..
Epilepsy and maladjusted personality	1	..	..
Epilepsy and alcoholism	1	..	..
Totals	5	1	1

illness or injury were compared, the level of significance as revealed by the χ^2 test fell between 5 and 2 per cent. The first comparison may be regarded statistically as strongly suggesting that the two distributions differ, while the second is acceptable as indicating that a true difference does exist.

Thus these data indicate that the abnormal electroencephalograms are related both to the selected factors in the family history and to illness or injury sustained early in life. When both factors are present, the level of significance is higher than when either factor operates alone.

The further problem then appears: Are certain of the selected criteria for a positive family

history, or for the personal history of illness or injury of the patient, closely related to electroencephalographic abnormality, and are certain others not? The data pertaining to this question are presented in tables 3 and 4. The number of cases is too small to allow the application of statistical technics; yet by inspection the data are of interest. Table 3 presents a summary of the electroencephalographic data in relation to the four selected categories of disorders in the family history: psychosis, maladjusted personality, chronic alcoholism and epilepsy. Two groups of patients, those in whose family history there was either epilepsy or maladjusted personality, stand out as having a relatively higher percentage of abnormal electroencephalograms than the other two groups.

TABLE 4.—*Analysis of the Electroencephalogram in Relation to Antecedent Illness or Head Injury*

	Electroencephalograms		
Illness or Injury	Abnormal	Questionably Normal	Normal
Prematurity and birth injury...	2	..	1
Prematurity and head injury...	1	..	..
Totals	3	..	1
Birth injury	1	..	1
Birth injury and prematurity...	2	..	1
Birth injury and severe illness...	1	..	2
Birth injury and convulsions....	..	..	2
Totals	4	..	6
Head injury	1	..	..
Head injury and prematurity...	1	..	..
Head injury and severe illness...	2	1	..
Head injury and convulsions....	1	..	..
Totals	5	1	..
Severe illness	8	..	6
Severe illness and birth injury...	1	..	2
Severe illness and head injury...	2	1	..
Severe illness and convulsions...	1	..	..
Totals	12	1	8
Convulsions	2	..	..
Convulsions and birth injury...	..	..	2
Convulsions and head injury....	1	..	..
Convulsions and severe illness...	1	..	..
Totals	4	..	2

Table 4 presents a summary of the electroencephalograms in relation to the five selected categories for illness and injury in the personal history: prematurity, birth injury, head injury, severe illness and convulsions. It is here seen that head injury is more closely associated with electroencephalographic abnormality than are the other factors. Whether these differences in tables 3 and 4 are due to chance or are true differences cannot be stated until further data are at hand, but the implications are worthy of investigation.

COMMENT

All the data which have been reported on the electroencephalographic abnormalities associated with primary behavior disorders in children suggest that that category may be subdivided into two types: primary behavior disorders with normal electroencephalograms and primary behavior disorders with abnormal electroencephalograms. The present data add another confirmatory link to a long chain of such evidence. In addition, they suggest the excellent probability that the second type can itself be further divided into two, or perhaps three, subtypes: one in which the abnormal electroencephalogram may be related to the family history, and thus by inference is probably hereditary; a second, related to illness or injury, sustained early in life (and of such a nature as to have been considered noncontributory to the behavioral disturbance), and a third, in which both factors may be believed to operate. Confirmation of the first of these proposed additional subtypes can be obtained directly, by investigations in which the electroencephalograms of both the parents and the progeny are recorded and are correlated with the family history. It is probable that some parents not considered to furnish "positive" evidence according to the evaluation of the social histories will show abnormalities in the brain potentials, the presence of which will extend the scope of the hereditary implications of the abnormal electroencephalogram. At present we are engaged in such an undertaking.

The implications of the abnormal record are clear, for one can only conclude that there is some pathophysiologic cortical process. The implications of the normal electroencephalogram are, in a sense, equally clear, that there is no pathophysiologic cortical process. It is of course necessary that these implications be considered in terms of the probability theory, for it is known that such a process may be dormant at the time of recording, and thus not be made apparent on the record. Furthermore, assumptions of the presence or absence of a pathophysiologic process can at present be referred only to the cortex. Subcortical processes may not be normal; yet the electroencephalogram may be repeatedly without discernible abnormal activity. (Deep lesions, for example, may be proved to be present and the electroencephalogram be normal.) Therefore one must consider the probability that an unknown number of patients present primary behavior disorders with normal electroencephalograms and still have pathologic neural function.[10]

10. These statements are not in exact accord with the recent experimental observations of Kennard (Effects on the Electroencephalogram of Chronic Lesions of Basal Ganglia, Thalamus, and Hypothalamus of Monkeys, J. Neurophysiol. **6**:405-415, 1943) on the mon-

(Footnote continued on next page)

Such a pathophysiologic process may be causally ascribed to several possible factors. Schreiber [11] presented evidence indicating that of 500 children showing neuropathologic changes, 70 per cent had had a period of prolonged apnea at birth. This clinical finding has been substantiated by direct experimental test, by Windle and Becker,[12] with the guinea pig as subject. Another factor has been indicated by Lurie and Levy,[13] who reported that the occurrence of pertussis before the age of 2 years is of importance in determination of subsequent patterns of behavior. Hence, perhaps more emphasis may be placed on factors of previously unsuspected or nonevaluated importance, particularly in cases in which the electroencephalogram does not meet standards of normality.

This approach appears definitely organic, but one can never successfully deny the tremendous importance of the social environment on the developing organism. However, unless the environment is limited and rigid, the individual organism has some freedom of selection from among the various social environments which present themselves to him. Out of this variety a child can choose that which meets his needs. Hence, a poor environment surrounding a given child may be the result of factors influencing his processes of selection (his own motivational processes, or needs). Furthermore, the child does make an impact on his social surroundings, and the impact involves energy on both sides of the equation: The environment acts back on the child according to the characteristics of the impact initiated by him. In turn, there is, then, further impact on the reacting environment, and a great spiral of activity takes place. Even if the initial impact is that of society on the child, the individual factors present within the child determine the consequent development of the spiral reacting processes.

The electroencephalographic data appear to indicate that there are discoverable and repeatedly verifiable organic processes in some of the heterogeneous group of disturbances diagnostically categorized as primary behavior disorders. If these organic processes are regarded as contributory to the disorder, such evidence affords considerable support to persons who subscribe to a view of constitutional determination of behavior patterns. However, the present data suggest that these constitutional variables be so defined as to include genogenic factors and characteristics acquired early in life, as a result of chemogenic or histogenic experiences which permanently alter the response tendencies of the organism. It has been proposed [14] that the pattern of the electroencephalogram is determined constitutionally, but it has been suggested [15] that such arguments should be limited to specific frequency bands of the electrocortical continuum which are known to be related to genogenic, histogenic and chemogenic factors. With such a restriction, it follows that abnormal (i. e., excessive slow or fast) activity may represent some aspect of the neural limits of the behavior of the organism, i. e., the variables limiting the range of the selection process and the variables determining the environmental tolerance levels.

We conclude from our data that these neural limits may be set by genetic and certain environmental factors and that the evaluation of a given patient depends entirely on the relative strength of the evidence in each of the possible contributory spheres: ancestral transmission, early physical trauma and social trauma.

CONCLUSIONS

1. As has frequently been shown, there is a high incidence of abnormality in the electroencephalograms of children with primary behavior disorders. In the present series of 67 children, none of whom presented signs of organic disease or in whose condition an organic etiologic factor was suspected, 49 per cent had electrical brain potentials which were clearly abnormal.

2. Age and sex were unrelated to electroencephalographic abnormality.

3. Significantly greater proportions of abnormal electroencephalograms were found when there was either a history of psychosis, maladjusted personality, chronic alcoholism or epilepsy in the family or a personal history of cerebral trauma or severe illness than when neither of these factors was present.

key, which indicate that induced cortical lesions may have no reflection in the electroencephalogram, while lesions in the thalamus and hypothalamus may indeed be reflected in the electrocortical records. There seems, therefore, to be disparity between clinical experience and experimental fact.

11. Schreiber, F.: Apnea of the Newborn and Associated Cerebral Injury, J. A. M. A. **111**:1263-1269 (Oct. 1) 1938.

12. Windle, W. F., and Becker, R. F.: Asphyxia Neonatorum: Experimental Study in the Guinea-Pig, Am. J. Obst. & Gynec. **45**:183-200, 1943.

13. Lurie, L. A., and Levy, S.: Personality Changes and Behavior Disorders of Children Following Pertussis, J. A. M. A. **120**:890-894 (Nov. 21) 1942.

14. Davis, H.: Some Aspects of the Electrical Activity of the Cerebral Cortex, in Cold Spring Harbor, Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1936, vol. 4, pp. 285-291.

15. Knott, J. R.: Electroencephalography and Physiological Psychology: Evaluation and Statement of Problem, Psychol. Bull. **38**:944-975, 1941.

SUBDURAL SUPPURATION ORIGINATING IN PURULENT LEPTOMENINGITIS

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In the course of routine autopsies we have observed occasional cases of subdural suppuration (figs. 1 and 2) which is apparently secondary to an underlying leptomeningitis. We wish to eliminate from this discussion all cases of subdural infection secondary to causes other than underlying disease of the leptomeninges. Specifically, we exclude subdural suppuration secondary to extension from diseased paranasal sinuses, mastoid air cells and the middle ear. Similarly, we exclude from consideration subdural infection arising from a penetrating cranial injury, infected subdural hematoma and osteomyelitis of the skull.

REVIEW OF LITERATURE

A diligent search of the literature failed to reveal any papers on this subject except for a single article by Bateman, in 1929.[1] In this report there is a passing reference to subdural suppuration secondary to involvement of the pacchionian granulations in cases of purulent leptomeningitis.

PRESENTATION OF CASES

In a series of 95 consecutive cases of leptomeningitis encountered in a total of 4,756 autopsies at the Queens General Hospital, only 2 with subdural involvement satisfied our previously stated criteria. Although apparently rare, subdural suppuration probably occurs much more frequently than our figures indicate. More careful gross and microscopic examination of the dura in all cases of leptomeningitis should bear out this assumption.

CASE 1.—A white man aged 61 was admitted to the hospital one month before his death with the complaint of weakness and eructation. The past history was noncontributory. The history of the present illness was unclear and largely irrelevant, as the patient had neither signs nor symptoms of meningitis at the time of admission. Recurrent attacks of painless jaundice had been present for six months. This was followed by the eventual development of the classic signs of neoplastic obstruction of the common bile duct.

Physical examination on admission revealed emaciation, cachexia and anemia, with a tender mass in the right upper part of the abdomen and a palpable liver.

The patient was awaiting operation when his temperature suddenly rose to 101 F. and then to 105 F. He complained only of headache, first mild and then severe. The following day he fell out of bed. When picked up, he seemed confused and disoriented. Examination showed no signs of injury, although he groaned when his head was moved. Ten hours later he passed into shock, and pulmonary edema developed, the patient dying almost immediately.

Fig. 1.—Subdural suppuration, gross appearance.

Necropsy failed to reveal any signs of cerebral trauma. The inner surface of the dura presented an adherent purulent membrane, measuring 10 by 6 by 0.2 cm., over the left parietal region. The subdural space contained a marked excess of cloudy fluid, from which a type VIII pneumococcus was recovered. There was a thick green subarachnoid exudate over the vertex and the cerebellum. The sphenoid sinuses and the middle ears were normal. The left ethmoid sinus contained a drop of cloudy fluid, from which Bacillus coli was cultured. Autopsy revealed that there was no connection between this infection and the subdural exudate.

From the Department of Pathology, Queens General Hospital.

1. Bateman, J. F.: Meningitis with Special Reference to the Role of the Pacchionian Bodies, Ohio State M. J. **25**:970-976, 1929.

The other autopsy observations were severe pancreatitis, with pronounced fibrosis and tendency to abscess formation, and a small carcinoma of the head of the pancreas, partially obstructing the common bile duct.

Microscopic examination confirmed the gross observation of subdural and leptomeningeal infection. The pacchionian granulations were intensely involved in the inflammatory process, with extension into the subdural space (fig. 3 *A* and *B*).

CASE 2.—A white boy aged 3 years was admitted to the hospital seven weeks before his death. The history was noncontributory. The child was admitted moribund and with great respiratory difficulty. Only a hurried physical examination was possible. An emergency tracheotomy was performed. For several days after the operation he had a high temperature. The fever could not be adequately explained, as the only physical signs during this interval were those of a mild infection of the upper respiratory tract. There were no signs of otitis media. On the seventh day he had obvious meningitis. Haemophilus influenzae was grown from the purulent spinal fluid. For the next six weeks he showed evidence of chronic purulent meningitis, with no decided change in his condition. Culture of repeated specimens of the spinal fluid yielded the same organism. At the end of six weeks he became worse suddenly, passing into coma and showing rigidity of the extremities, especially on the left side. After this sudden change, the course was rapidly downhill, death occurring after seven weeks of illness.

Necropsy revealed a 2 cm. area of adhesions between the dura and the arachnoid over the right frontal region. Microscopic sections taken through this area showed a purulent exudate in both the subarachnoid and the subdural spaces. The arachnoid membrane was necrotic and partially destroyed. Diffuse purulent leptomeningitis with prominent hydrocephalus was also present. The middle ears and the sinuses were free of infection. Of particular interest was the necrotizing involvement of the bridging vessels, particularly the veins, which in some cases had allowed their infected contents to escape through their damaged walls (figs. 2 and 4).

In 3 other cases of our series we observed subdural purulent inflammation together with purulent leptomeningitis. A complicating factor in each of these cases was the presence of a coexistent infection of the middle ear or the paranasal sinuses. In each case we were able to culture a pneumococcus from both the subarachnoid and the subdural spaces, and significantly, we could culture only a streptococcus, a staphylococcus or Bacillus pyocyaneus from the middle ear or the sinuses. Therefore we are certain that these cases represent an extension of antecedent leptomeningitis into the subdural space. However, because of the complicating

Fig. 2 (case 2).—Subdural empyema following necrosis of the arachnoid with extension into the subdural space; × 100.

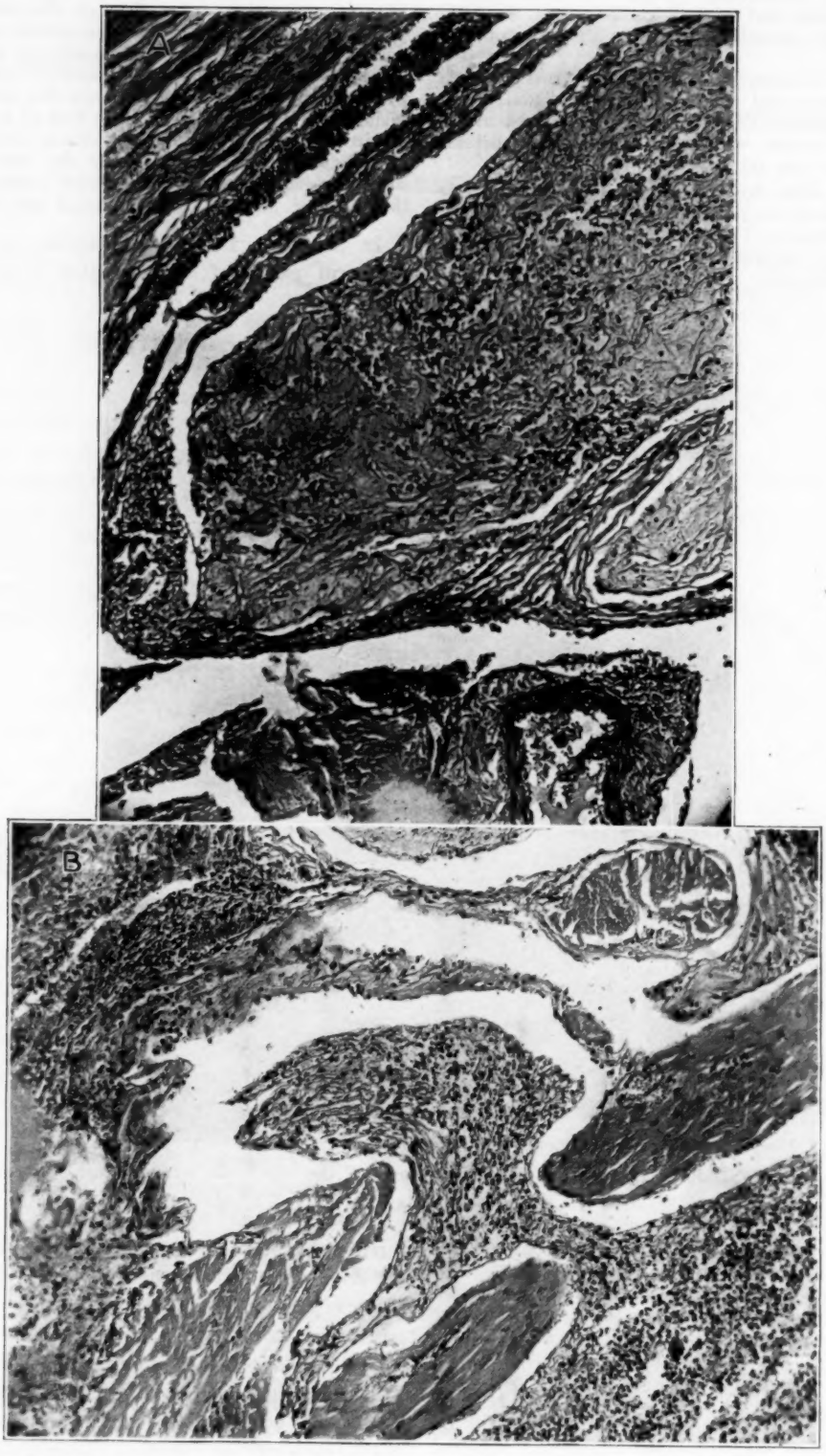

Fig. 3 (case 1).—*A*, massive involvement of the arachnoid villus, with beginning extension into the subdural space. *B*, massive involvement of the arachnoid villus, with beginning extension into the subdural space; × 100.

infection of the sinus or the middle ear, they fail to satisfy the introductory criteria for inclusion in our group of cases.

PERTINENT ANATOMIC RELATIONS AND MECHANISMS OF EXTENSION

The gross and microscopic anatomy of the meninges has been described by Weed [2] in some detail. However, a brief review of the pertinent histologic features, with especial reference to the mesothelial elements involved, will serve to clarify further discussion (fig. 5).

Fig. 4 (case 2).—Extensive phlebitis in a bridging vein; × 440.

The brain is covered by three membranes. The innermost layer, the vascular pia, is applied directly to the surface of the brain. The outer layer of the pia consists of a single, incomplete layer of mesothelial cells (*A*). The second membrane, the arachnoid, consists of connective tissue covered on the inner aspect by an incomplete layer of mesothelial cells (*B*). This mesothelium is continuous with similar mesothelium covering the trabeculae and blood vessels which traverse the subarachnoid space. The outer layer of the arachnoid, which is applied to the inner layer of the dura, consists of a complete mesothelial sheet (*C*). It is the subarachnoid space which contains the cerebrospinal fluid. The third membrane, or dura mater, consists of several layers of connective tissue with an innermost, complete mesothelial membrane (*D*). The outer surface of the dura is attached to the bones of the skull and is firmly adherent to the suture lines. The subdural space is therefore a potential space between two complete mesothelial membranes investing the outer aspect of the arachnoid and the inner surface of the dura (*E*).

The dural sinuses are venous channels lined by endothelium and formed by triangular separations of the layers of the dura. Along the dural sinuses, particularly the superior sagittal sinus, there are numerous outpouchings of arachnoid and mesothelium, known as arachnoidal villi (*F*). These villi project into the lumen of the sinuses and, in addition to their component

2. Weed, L. H.: An Anatomical Consideration of the Cerebrospinal Fluid, Anat. Rec. (supp.) **12**:461, 1917.

arachnoid connective tissue and mesothelium, are covered by layers of dural mesothelium and sinus endothelium. Consequently, the potential subdural space can be considered as continuous over the arachnoid villi and is separated from the interior of the villus by only two layers of mesothelium, one of which is incomplete.

The subarachnoid and subdural spaces are generally considered to have no points of communication. However, the arachnoid villi and the bridging veins act as potential paths of communication. Our low proportion (2 per cent) of cases of complicating subdural suppuration seems to indicate that the arachnoid membrane

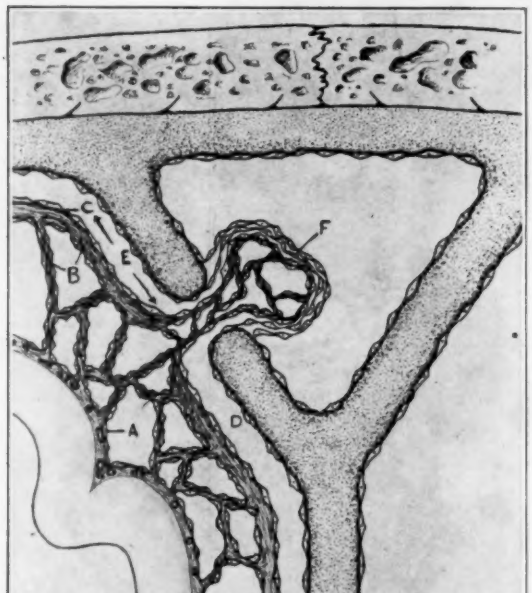

Fig. 5.—Diagrammatic representation of the layers of the meninges. *A*, outer layer of pia (incomplete layer of mesothelial cells); *B*, inner layer of arachnoid (incomplete layer of mesothelial cells); *C*, outer layer of arachnoid (complete layer of mesothelial cells); *D*, inner layer of dura (complete layer of mesothelial cells); *E*, subdural space, and *F*, arachnoid villus.

is an effective barrier to the spread of infection, despite its tenuous nature.

From a study of our autopsy material, we have derived several methods of possible spread from the subarachnoid space into the subdural space.

The first, and most obvious, mechanism is that of direct extension through the arachnoid membrane (fig. 2). This may occur in cases of chronic leptomeningitis or of leptomeningitis caused by organisms with unusual cytolytic powers. In none of our cases was the infection due to the meningococcus, the most common cause of leptomeningitis.

The second possible method of extension into the subdural space is through the medium of the arachnoid villi (fig. 3 *A* and *B*). Bateman[1] claimed that the villi are involved in every case of leptomeningitis. This is to be expected, since the villi are simply protruding extensions of the subarachnoid space. As the result of massive involvement of the arachnoid villi, necrosis of the boundary membranes may occur, permitting the escape of infected contents into the subdural space. With less severe involvement of the villi, the selective permeability of the membrane may simply be disturbed enough to permit the passage of bacteria, without actual destruction of the membrane barrier. Bateman showed that infection of the subdural space immediately adjacent to the arachnoid villus is not unusual. In our own experience, in most cases of purulent leptomeningitis the arachnoid villi show massive involvement, although gross extension into the subdural space has been seen only rarely.

A third possible mechanism of extension is involvement of the bridging veins (fig. 5). These veins traverse both the subarachnoid and the subdural spaces and, because of their incomplete covering of mesothelium, may readily be infected with purulent leptomeningitis.[3] Once there are involvement of the vessel wall and a resultant septic thrombus, the infected contents may be transmitted into the subdural space through necrosis of the vessel wall.

Another possible method of extension, which we have not seen, consists of thrombophlebitis of the bridging veins, resulting in secondary thrombosis of the sinus with retrograde involvement of the subdural space over the pacchionian granulations.

The fifth possible mechanism of extension is the inoculation of both the arachnoid and the dura by a blood-borne infection, with simultaneous involvement of both membranes. We have never seen this occur and mention it only for completeness.

We have purposely omitted from consideration the obvious artificial contamination of the subdural space resulting from spinal or cisternal puncture. In our first case no subarachnoid drainage whatever was performed. In the second case there was subdural infection over the dorsum of the brain, with no infection in the region of the puncture. The latter condition eliminated the possibility of artificial contamination.

3. Courville, C. B.: Subdural Empyema Secondary to Purulent Frontal Sinusitis, Arch. Otolaryng. **39**: 211-230 (March) 1944.

CLINICAL APPLICATION

The occurrence of subdural infection is clinically important both as a serious immediate complication of leptomeningitis and as a possible cause of postmeningitic epilepsy at some future date. It is well known that epilepsy is not an uncommon sequel to meningitis following otitis media, particularly when the meningitis is caused by a pneumococcus, a streptococcus or a staphylococcus. However, epilepsy is a most unusual complication of the ordinary meningococcic meningitis. This may be due to the fact that subdural empyema is a not infrequent complication of meningitis caused by a gram-positive coccus, but rarely follows meningococcic meningitis. Ney [4] showed conclusively that the presence of scar tissue between the dura, the arachnoid and the brain tissue produces traction on the brain, as a result of the dura's inelasticity and rather firm fixation to the skull. He stated the theory that the area of cortex on which traction is exerted gradually becomes increasingly irritable, eventually constituting an epileptogenous zone. These adhesions can be demonstrated by roentgenographic technics developed by Ney. Confirmatory proof of the causal relation of these adhesions to the occurrence of epilepsy has been obtained at operation by tugging on the adhesion and initiating an epileptiform seizure. In contrast to the occasional dramatic symptoms produced by adhesions between the dura, the arachnoid and the cortex, the adhesions between the arachnoid and the brain substance alone are of little apparent significance. Such adhesions are frequently a purely incidental observation at autopsy in cases with no history of convulsions.

In view of its serious consequences, therefore, it is important to bear in mind the possible occurrence of subdural empyema, particularly in chronic purulent leptomeningitis or in the leptomeningitides caused by the gram-positive cocci or by H. influenzae. Diagnosis must be made early. Courville [3] discussed the symptoms in some detail. Conspicuous features of subdural extension are severe persistent headache and general signs of sepsis out of proportion to the localizing signs. No program of treatment has yet been applied; however, it is suggested that penicillin with surgical drainage may prove of value. The existence of this lesion has an important bearing on the prognosis of leptomeningitis, both because it acts as a seeding focus for sepsis and because it may produce pressure atrophy of the cortex. Its possible occurrence should be kept in mind.

CONCLUSIONS

1. Subdural suppuration appears as a rare complication of purulent leptomeningitis, although a higher incidence will undoubtedly be revealed as a result of more complete autopsy studies.

2. Several possible mechanisms of the spread of infection from the subarachnoid to the subdural space exist.

3. This condition has significance both as an immediate serious complication and as a possible cause of postmeningitic epilepsy.

4. It is noteworthy that this complication did not occur with meningococcic infection, the most common cause of leptomeningitis.

4. Ney, K. W.: Pathologic Factors in the Production of Traumatic Epilepsy, J. M. Soc. New Jersey **40**: 270-275, 1943.

HYPERTHERMIA FOLLOWING INJURY OF THE PREOPTIC REGION

REPORT OF A CASE

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Acute cerebrogenic hyperthermia has long been recognized as an entity of neurosurgical importance (Cushing,[1] Gagel,[2] Dott,[3] Erickson,[4] Davison [5] and Zimmerman [6]). Clinical accounts have indicated that this type of high, and often fatal, fever is caused by injury of the hypothalamus or of nearby parts of the brain, a general conclusion in accord with the results of recent animal experimentation. However, in most instances of neurogenic hyperthermia in man the cerebral damage has been diffuse, and localization of the responsible region has not been as precise as that achieved by special technics in animals. The most discrete lesions described in the literature are those presented by Alpers.[7]

The following case is thought worthy of record because the injury of the brain that was believed to have destroyed central mechanisms for heat loss and thus have resulted in the extreme elevation of body temperature was more circumscribed than the lesion noted in any other report with which we are acquainted.

1. Cushing, H.: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C Thomas, Publisher, 1932.

2. Gagel, O.: Symptomatologie der Erkrankungen des Hypothalamus, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 5, pp. 482-522.

3. Dott, N. M.: Surgical Aspects of the Hypothalamus, in Clark, W. E. L.; Beattie, J.; Riddoch, G., and Dott, N. M.: The Hypothalamus, London, Oliver & Boyd, Ltd., 1938, pp. 131-185.

4. Erickson, T. C.: Neurogenic Hyperthermia (A Clinical Syndrome and Its Treatment), Brain **62**:172-190, 1939.

5. Davison, C.: Disturbances of Temperature Regulation in Man, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:774-823, 1940.

6. Zimmerman, H. M.: Temperature Disturbances and the Hypothalamus, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:824-840, 1940.

7. Alpers, B. J.: Hyperthermia Due to Lesions in the Hypothalamus, Arch. Neurol. & Psychiat. **35**:30-42 (Jan.) 1936.

REPORT OF CASE

History.—A white infantry soldier, appearing to be in his early thirties, was brought to an evacuation hospital in a forward zone on March 17, 1944, at 9:50 a. m. He had been struck by a mortar shell fragment, which had inflicted a lacerated gutter wound of the right temple. Because of severe combat conditions no associates could be reached for a detailed account of the way in which the injury was incurred. From the ambulance driver it could only be learned that the patient had been hit thirty to sixty minutes prior to the time of admission, that he had become immediately unconscious and that he had been given ½ grain (0.032 Gm.) of morphine sulfate hypodermically.

He had been taken to the shock ward and had received 1 unit of plasma before he was examined.

Examination.—The patient was in coma and did not react to painful stimulation. He was well nourished and well developed, and physical examination revealed no abnormalities except the wound in the head. The oral temperature was 98.6 F., the pulse rate 80 and the respiratory rate 16 per minute, and the blood pressure was 120 systolic and 60 diastolic. A 4 inch (10 cm.) gash extended horizontally across the right temple. Torn muscle was exposed. Neurologic examination demonstrated active and bilaterally equal deep reflexes and brisk superficial reflexes. The Babinski toe sign was elicited in each foot. There was no papilledema. The pupils were fixed at 2.5 mm. An emergency roentgenogram of the skull disclosed no evident fracture.

Course of Illness.—With the use of local infiltration with procaine, the scalp and temporal muscle were debrided, and the wound was closed. At noon, when the patient was next visited, his oral temperature had risen to 100 F. He had become completely vegetative, and no reflex responses could be obtained. The pulse rate was 100 and the respiratory rate 6 to 8 per minute, with periods of apnea. The pupils were still fixed at 2.5 mm. By 3 p. m. the breathing was further slowed and more irregular, and the oral temperature had reached 106.4 F. The pupils were unchanged. An unsuccessful attempt had been made to reduce the fever by sponging with cold water.

After a review of the history to this point, a diagnosis of cerebral laceration with subdural hematoma was made. As soon as an operating table was free, he was taken to the surgical tent. At 6 p. m. an osteoplastic craniotomy was done in the right temporal region. An extensive epidural hemorrhage was encountered, and incision of the dura mater revealed a fresh, massive temporoparietal subdural hematoma. When the latter was removed by suction, the under-

lying cortex was seen to be covered with widespread subpial hemorrhage. As an attempt was being made to control the bleeding from the middle meningeal artery, the patient suddenly stopped breathing and shortly died, in spite of artificial respiration. A few moments before death respiration had seemed more regular. The terminal rectal temperature was 108.2 F.

Necropsy. — Postmortem examination, which was made at once, revealed no pathologic changes except those of the skull and its contents. Two roughly vertical, linear breaks of the right temporal squama, crossing the squamosal suture into the inferior portion of the parietal bone, were discovered. (On reexamination of the roentgenograms one of these fractures could be made out.) The more anterior of the fractures connected with a fracture line which ran over the petrosal part of the temporal bone, traversing the arcuate eminence and ending over the internal acoustic meatus. The middle meningeal artery was torn in a wing of this crack, which ran toward the foramen spinosum.

Inspection of the brain showed extensive contusion and slight laceration on both sides of the right lateral cerebral fissure and an area, oval and 2 inches long, of more severe cortical laceration of the right middle temporal gyrus. After removal of the hemispheres it was seen that the dura mater lining the right middle cranial fossa was finely streaked with blood, as though the dura mater itself was bruised. This was most pronounced anteriorly, on the cerebral face of the greater wing of the sphenoid bone.

The brain was sectioned immediately, since no facilities for preservation were available. No ventricular hemorrhage was present. There was no damage to the brain stem except for slight softening of the central gray matter of the mesencephalon at the level of the inferior colliculus. In the left hemisphere a long, stablike hemorrhage ran through the caudate nucleus and into the upper part of the internal capsule, from a frontal level of the anterior commissure to a frontal level of the middle of the thalamus. There was no other injury of the basal ganglia.

The only other lesion, and the one which seemed most significant, was a localized softening of the preoptic region, on both sides of the optic recess of the third ventricle, between the optic chiasm and the anterior commissure. This area did not widen as far laterally as the globus pallidus at any point. Posteriorly it was sharply delimited and did not involve the tuberal portion of the hypothalamus. Anteriorly it extended to the limit of the preoptic substance.

COMMENT

This case by no means presents final evidence that the division of the brain principally damaged, the preoptic area, is the center containing neural mechanisms for control of heat loss in man, destruction of which results in neurogenic hyperthermia. First, unfortunately, the patient was seen in a battle situation which precluded adequate investigation of the brain. It is possible that microscopic study of prepared material would have disclosed other pathologic changes. Second, the patient was wounded and treated in a tropical theater of war, and high environmental temperature may have played a role in the development of his fever. However, the temperature on the day of his hospitalization was in the middle eighties, and we do not believe it was a factor. No case of hyperthermia was noted among many other men with severe head injuries who were cared for under the same climatic conditions. Third, epidural and subdural hemorrhage produced general encephalic compression, and other areas of cerebral damage of the midbrain, the caudate nucleus, the internal capsule and the temporal and frontal cortex, existed. Yet none of these regions, or any combination of them, has to our knowledge, ever been implicated as an anatomic factor in the production of cerebrogenic fever.

Perhaps an attempt should have been made to reduce the fever with pentobarbital sodium, as suggesaed by Beaton, Leininger, McKinley, Magoun and Ranson,[8] or with other drugs (Erickson [4]). The extreme embarrassment of respiration was the factor which decided us against pharmacologic intervention. If operation had been successful and respiration had improved, administration of pentobarbital sodium would have been tried.

The particular interest of this case lies in the localization of the lesion presumably accounting for the elevated temperature to a small part of the brain, the preoptic region. In the monkey, local heating of this area with high frequency currents results in the activation of mechanisms for heat loss (Beaton, McKinley, Berry and Ranson [9]), while circumscribed destruction of the area causes central paralysis of these processes and consequent fatal hyperthermia (Beaton, Leininger, McKinley, Magoun and Ranson [8]). In spite of the limitations on pathologic study imposed by the conditions under which the case was observed, the results seem to lend credence to the supposition that in man, also, the site of central mechanisms for heat loss is the preoptic region.

SUMMARY

A case of injury of the preoptic region with subsequent development of neurogenic hyperthermia presents evidence that this area contains the specific neural mechanisms for heat loss in man.

8. Beaton, L. E.; Leininger, C.; McKinley, W. A.; Magoun, H. W., and Ranson, S. W.: Neurogenic Hyperthermia and Its Treatment with Soluble Pentobarbital in the Monkey, Arch. Neurol. & Psychiat. **49**:518-536 (April) 1943.

9. Beaton, L. E.; McKinley, W. A.; Berry, C. M., and Ranson, S. W.: Localization of Cerebral Center Activating Heat-Loss Mechanisms in Monkeys, J. Neurophysiol. **4**:478-485, 1941.

Minor Notes

DETECTION OF LATENT EXTENSOR PLANTAR REFLEX

ALFRED GORDON, M.D., PHILADELPHIA

Margolis and Graves[1] have described a method to facilitate the detection of the latent Babinski sign. Injection of a strong dose of scopolamine hydrobromide produces the desired reflex when there is doubt as to the organic nature of the condition in a given case. The authors' investigations cover a sufficiently large number of patients to justify them in the assumption that in "none of the aforementioned patients did a latent Babinski sign appear in the absence of damage to the pyramidal tract." They cite a number of authors who used this test to bring out a latent pyramidal sign, although the majority experimented only in cases of parkinsonism. The latter disease is, of course, essentially a pathologic condition of the extrapyramidal system. Nearly all authors have claimed that the pyramidal involvement is only a subsequent complication and that when the plantar reflex is evoked in extension with scopolamine there must be involvement of the pyramidal system. .

Special attention is called to Link's work on induction of narcosis in mentally deranged patients, to whom scopolamine was invariably given with morphine. The question arises which of the two drugs was responsible for evoking an extensor plantar reflex or perhaps whether both could be incriminated. Volkmann observed the extensor plantar reflex in patients anesthetized with scopolamine and morphine for surgical operations. Zador obtained the reflex response not only in patients with postencephalitic parkinsonism but in normal persons who were given scopolamine in doses over 1 mg.

At this juncture I refer the reader to a previous communication.[2] Briefly, a middle-aged man with a normal nervous system received from a pharmacist a potion containing morphine for relief from an attack of his usual rheumatism. The amount of morphine sulfate was a little over 1 grain (0.065 Gm.). Half an hour later he became comatose. When he regained consciousness, he noticed he could not walk easily. On examination at the Jefferson Hospital, I observed a typical picture of spastic paraplegia, with a notably increased patellar reflex, ankle clonus and extensor plantar reflex. Seventeen hours later all the symptoms of lateral sclerosis disappeared. It is evident that degeneration of the motor tract is not necessary to produce the aforementioned symptoms. One is forced to infer that irritation or functional disturbance from any cause is sufficient to evoke pathologic phenomena referable to the motor tract.

In the case just described toxicity (morphine poisoning) probably produced the irritation of the pyramidal tract in the spinal cord. In cases of epileptic coma (not of jacksonian type) I have frequently observed an extensor plantar reflex, which disappeared on recovery from the coma. In cases of chronic alcoholism the presence of an extensor plantar reflex is probably due at first to the toxic effect of alcohol on the motor cortex and later, by reason of chronicity, to secondary organic changes.

There is no doubt that the scopolamine test is a valuable aid in detection of organic changes in the pyramidal tract in doubtful cases, but an extensor plantar reflex may be elicited also in persons with a normal nervous system when it is exposed to irritating toxic elements.

1. Margolis, L. H., and Graves, R. W.: Detection of the Latent Babinski Sign with Scopolamine, Arch. Neurol. & Psychiat. **52**:409 (Nov.) 1944.

2. Gordon, A.: Spinal Symptoms Caused by Acute Morphine Poisoning, Philadelphia M. J. **11**:497 (March 21) 1903.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

UTILIZATION OF OXYGEN BY THE BRAIN IN TRAUMATIC SHOCK. A. BLALOCK, Arch. Surg. **49**:167 (Sept.) 1944.

In anesthetized dogs shock was produced by hemorrhage, trauma, burns and tourniquets, and the oxygen contents of the blood obtained from the femoral artery, the right auricle and the cerebral venous sinuses were determined. In the state of shock there was usually an increase in the difference between the oxygen content of arterial and that of cerebral venous blood even before the blood pressure began to drop. Under conditions of decreasing blood flow the brain, unlike the kidneys, appears to maintain its oxygen consumption, at least partially, by extracting increased amounts of oxygen from the arterial blood.

LIST, Ann Arbor, Mich.

NON-PROTEIN NITROGEN AND PROTEIN CONCENTRATIONS OF SERUM AND CEREBROSPINAL FLUID IN SHOCK. GEORGE W. DUNCAN, J. LOGAN IRVIN and STANLEY J. SARNOFF, Bull. Johns Hopkins Hosp. **75**:135 (Aug.) 1944.

Duncan, Irvin and Sarnoff report observations on the nonprotein nitrogen and protein concentrations of the serum and the cerebrospinal fluid in dogs subjected to experimental shock produced by a crushing injury to a limb. These observations were compared statistically with data obtained from a control group of dogs.

The authors observed that the mean concentrations of both nonprotein nitrogen and protein in the serum and the cerebrospinal fluid were significantly greater for the animals subjected to trauma. The mean ratios of the concentrations of nonprotein nitrogen in the serum to the corresponding concentration in the spinal fluid were 1.58 for the controls and 2.02 for the animals in shock. The mean ratios of the concentration of protein in the serum to the corresponding concentration in the cerebrospinal fluid were essentially the same for the two groups. These experiments indicate that if alteration in the barrier relation between plasma and cerebrospinal fluid does occur in shock produced by this method, it is not sufficient to permit extensive passage of plasma protein into the spinal fluid.

GUTTMAN, Philadelphia.

INTERACTION OF NEIGHBORING FIBERS IN MYELINATED NERVE. AMADEO S. MARRAZZI and RAFAEL LORENTE DE NÓ, J. Neurophysiol. **7**:83 (March) 1944.

Marrazzi and Lorente de Nó studied the sciatic nerve of the bullfrog to determine the changes in excitability of the fibers of the medial peroneal nerve after the administration of a two-thirds maximal shock to the lateral peroneal nerve. The results of the experiments were expressed in the form of interaction curves, the interaction being due to the flow of action currents of the active fibers through the membrane of the inactive fibers. The interaction current could be differentiated into two parts: an immediate and a residual interaction current, the latter outlasting the flow of the action currents. The residual interaction current had an electric sign consisting of a change in membrane potential. The shape of the interaction curve depends on the geometric conditions determining the low of the action current through the inactive fibers and on the temporal course of the stimulating fibers.

FORSTER, Philadelphia.

THE ELECTRICAL ACTIVITY OF REGENERATING NERVES IN THE CAT. CHARLES M. BERRY, HARRY GRUNDFEST and JOSEPH C. HINSEY, J. Neurophysiol. **7**:103 (March) 1944.

Berry, Grundfest and Hinsey under sterile conditions divided and then sutured the sciatic nerves, or the tibial and peroneal branches, of 58 cats. Evidence of return of motor and sensory functions was observed. At periods varying up to four hundred and sixty-six days acute experiments were performed and the effects of stimulation in situ determined. After this the nerves were excised, and the electrical response to stimulation and the histologic state of the nerves were determined.

The authors observed the presence of small, slowly conducted action potentials as early as seventeen days after operation. As the postoperative time became longer the potentials increased in size, velocity and complexity. The threshold for stimulation of regenerating fibers was high peripherally and low centrally with reference to the suture. In the course of time the peripheral threshold decreased. As the impulse passed the suture an abrupt drop in velocity occurred. In the fibers distal to the suture the return of conduction velocities was slow, and the increase in velocity was at a constantly decreasing rate. The return of maximum fiber diameter took a similar course. The relation of maximum fiber diameter to maximum conduction velocity was linear.

FORSTER, Philadelphia.

RELATION OF THRESHOLD FOR EXPERIMENTAL CONVULSIONS TO BODY WEIGHT. FEDERICO SAL Y ROSAS, Rev. neurol. de Buenos Aires **8**:302 (July-Sept.) 1943.

The relation of the minimum amount of metrazol necessary to cause a convulsion to body weight was studied in 204 subjects, 107 of whom were epileptic. On the whole, the convulsive threshold varied directly with the weight of the patient. The author emphasizes the significance of other factors, such as a history of epilepsy, a tendency to hysterical convulsions and the use of sedatives. The mean minimal dose for all patients who had been without phenobarbital for a long time was 5.5 mg. per kilogram of body weight, 4 mg. for epileptic patients and 6.3 mg. for nonepileptic patients. The minimal dose per kilogram of body weight is less for patients with conversion hysteria with a history of convulsive movements than for hysterical patients without such a history.

SAVITSKY, New York.

Neuropathology

CYSTICERCUS CELLULOSAE OF THE BRAIN. META A. NEUMAN, J. Neuropath. & Exper. Neurol. **2**:197 (April) 1943.

The case reported is that of an American aged 35, returned from the Orient, who had been hospitalized

in the United States for eight years and was suspected of having dementia paralytica. He had had the first convulsion nine years before death. In spite of intensive antisyphilitic therapy, he grew worse, and his convulsions became more frequent and severe. Neurologic examination suggested diffuse, chronic encephalomeningomyelitis. He finally died, with a a temperature of 108 F. Autopsy revealed numerous cysticerci scattered throughout the brain. As well as could be determined, the patient had never harbored an intestinal parasite.

Cerebral cysticercosis should be considered in the cases of adults who have lived in foreign countries and who have their initial convulsions relatively late in life.

CAMPBELL, New York.

NEUROHISTOLOGIC FINDINGS IN EXPERIMENTAL ELECTRIC SHOCK TREATMENT. N. W. WINKELMAN and MATTHEW T. MOORE, J. Neuropath. & Exper. Neurol. **3**:199 (July) 1944.

Winkelman and Moore report their observations in a study of 12 cats. One group, of 8 animals, was treated with the faradic shock modality used by Berkwitz, while the other group, of 4 animals, was treated with the modality advocated by Cerletti and Bini, using the Offner machine. Treatments were given three times a week. Most of the animals received a series of from ten to twenty shock treatments before they were killed. The nutrition of the animals was carefully controlled. The cats were killed by being bled while under ether anesthesia three days to ten weeks after the last treatment. The brain and cord of all the animals were removed immediately, fixed in a 4 per cent concentration of solution of formaldehyde U. S. P. for twenty-four hours and then cut and placed in alcohol. Sections were embedded in paraffin and pyroxylin, and frozen sections were made. The sections were stained with hematoxylin and eosin, toluidine blue, Weil's stain for myelin sheaths, Bodian's stain and scarlet red, while the Cajal and Hortega technics were employed for the various types of glia.

Histologic studies of the brain and cord of all the animals were made, many by serial sections. No morphologic changes were observed in animals receiving convulsive doses of electric current analogous to those given to patients. Two animals received excessive doses of electric shock. The brain of 1 of these cats showed a small area of pericapillary hemorrhage, while in the other some of the smaller blood vessels were congested. No instance of subarachnoid hemorrhage or diffuse or extensive intracerebral hemorrhages was noted.

Winkelman and Moore believe that when hemorrhages occur in the brain of an animal after electric shock convulsion one or more of the following factors were operative: (1) The intensity of the current was excessive as compared with the corresponding dose used with human subjects; (2) deprivation of vitamin B and C, and probably vitamin K, occurred during the course of treatment, and, finally, (3) craniocerebral injury, due to inadequate restraint and protection, was incurred during the convulsion.

GUTTMAN, Philadelphia.

THE PATHOLOGICAL CHARACTERISTICS OF EMBOLIC OR METASTATIC ENCEPHALITIS. BERNARD J. ALPERS and HERBERT S. GASKILL, J. Neuropath. & Exper. Neurol. **3**:210 (July) 1944.

Alpers and Gaskill report their observations in 17 cases of embolic encephalitis. Attention was focused on changes in the brain and the source of the embolic foci. The material was obtained from cases representing the following sources of the emboli: subacute bacterial endocarditis, 5 cases; acute vegetative endocarditis, 5 cases; bronchiectasis, 3 cases; pulmonary abscess, 1 case; gangrene of the foot, 1 case; retroesophageal abscess, 1 case, and osteomyelitis of the hip, 1 case. Sections were taken from all parts of the cerebral hemispheres, the brain stem and the cerebellum and were embedded in paraffin and pyroxylin. In many instances studies by serial section were made in order to study the origin and development of the encephalitic foci. Hematoxylin and eosin, toluidine blue, Weil's stain for myelin sheaths, Cajal's gold chloride stain for astrocytes, scarlet red for fat and, in some instances, Bodian's stain for axis-cylinders were employed.

The authors state that the commonest cause of metastatic encephalitis is bacterial endocarditis, particularly of the subacute variety. Acute endocarditis, pulmonary disease and infections of other organs may give rise to this type of encephalitis. The clinical manifestations indicating involvement of the brain, particularly in cases of endocarditis, may usher in the disease; they may be terminal or may occur at any time during the course of the illness.

The number of areas of encephalitis vary from a few to many. They occur in the cerebral hemispheres, the brain stem and the basal ganglia. Microscopic study reveals proliferative endarteritis, which tends to be generalized; areas of perivascular infiltration with leukocytes; minute leukocytic nodules, which are essentially miliary abscesses, and, in some instances, areas of petechial and perivascular hemorrhage. Subarachnoid, cerebral or ventricular hemorrhage may be seen, as well as meningitis.

Alpers and Gaskill conclude that metastatic encephalitis is probably due to blood-borne bacteria, which are probably disseminated by the system of paravertebral veins described by Batson.

GUTTMAN, Philadelphia.

ALTERATIONS IN BRAIN STRUCTURE AFTER ASPHYXIATION AT BIRTH: AN EXPERIMENTAL STUDY IN THE GUINEA PIG. W. F. WINDLE, R. F. BECKER and ARTHUR WEIL, J. Neuropath. & Exper. Neurol. **3**: 224 (July) 1944.

Windle, Becker and Weil report observations on the effect of asphyxia in guinea pigs. Proof that asphyxia leads to neurologic defects may never be found in the human newborn infant because adequately controlled conditions—multiple births—are uncommon. These animal experiments supplement clinical observations.

The experimental procedure in most instances was as follows: Pregnant guinea pigs at, or close to, term were operated on after the abdomen was anesthetized with a 1 per cent solution of procaine hydrochloride. One fetus of each litter was delivered without delay to serve as the control for the fetuses to be asphyxiated. The uterine blood vessels or the umbilical cord was then occluded with clamps to induce a state of hypoxia in the remaining fetuses. Violent movements, including respiratory activities in utero, were executed during the first stage of asphyxia. When their respiratory efforts ceased, the fetuses were delivered. The average duration of asphyxiation was a little over thirteen minutes (range, four and a half to twenty-one minutes). The average time required for resuscitation (with oxygen containing 10 per cent carbon dioxide) was twenty-

nine minutes (range, a few seconds to well over an hour) for the 66 animals selected for study. Some litters contained three or more animals, and two or more fetuses were asphyxiated; 50 controls were provided. Sixty-six of the newborn guinea pigs were resuscitated and lived thirty minutes to thirteen weeks. The brains of all the animals were preserved and sectioned serially. Observations were made on sections stained by various technics.

Multiple capillary hemorrhages, and occasionally larger hemorrhages, were noted in all animals which survived asphyxiation for three hours to five days. These lesions were observed in half the animals which survived from thirty minutes to two hours, while no lesions were observed in the animals which did not survive the period of asphyxia. There was a notable variation in the amount and distribution of the hemorrhages. However, hemorrhage was not considered the cause of extensive damage to the neurons.

Edema was present in the brains of all but 1 of the animals which survived eight hours to four days after resuscitation. After five days the edema subsided.

Cytologic changes were observed in all the brains of animals killed from one and one-half hours to twenty-one days after resuscitation. The usual sequence of events was clouding of the Nissl granule pattern, beginning one to two hours after resuscitation; swelling of some neurons and shrinkage of others in three hours; loss of stainability with thionin, appearing in about five hours; typical chromatolysis, in one or two days, complete lysis of neurons as early as four days after resuscitation and hyperchromatic staining in at least three weeks. Some specimens presented generalized changes throughout most of the brain, while others showed only focal abnormalities. The cerebellum and the corpus striatum were not notably affected, while the thalamus, cerebral cortex, tegmentum and spinal cord were often severely damaged.

Asphyxia induced a transient microglial reaction between two days and three weeks after resuscitation. Thereafter the glia assumed normal proportions.

Generalized or focal atrophy followed the loss of neurons in about two thirds of the severely asphyxiated animals and in one half of the mildly asphyxiated guinea pigs. As late as thirteen weeks after resuscitation neurons in the damaged brains stained darker and were more shrunken than the neurons in the brains of litter mate controls. Areas of partial necrosis occurred in 8 animals. Loss of myelin appeared to be secondary to loss of cells.

The authors conclude that experimental asphyxiation followed by successful resuscitation in guinea pigs at birth produced pathologic changes of variable degrees of severity in all specimens of the brain studied between one and one-half hours and three weeks after birth and detectable permanent anatomic changes in more than one-half the animals allowed to live more than three weeks.

GUTTMAN, Philadelphia.

A CASE OF ATYPICAL LINDAU'S DISEASE. W. R. BRAIN, J. G. GREENFIELD and D. W. C. NORTHFIELD, J. Neurol. & Psychiat. **6**:32 (Jan.-April) 1943

Brain and his associates report an unusual case of Lindau's disease without the presence of cerebellar tumor. The findings were a hemangioblastoma in one retina and two similar lesions in the other, a hemangioblastoma of the spinal cord associated with extensive syringomyelia and cysts of the pancreas and kidneys. There was evidence of hereditary transmission of the disease. According to most statistics, hemangioblastoma is more common as a primary tumor in the cerebellum than in the spinal cord, the cauda equina or the cerebral hemispheres. The syringomyelia was interpreted as a separate developmental anomaly.

MALAMUD, Ann Arbor, Mich.

Psychiatry and Psychopathology

PSYCHONEUROLOGCAL PROBLEMS RELATED TO THE SURGICAL TRANSSECTION OF THE PREFRONTAL ASSOCIATION AREAS IN MAN. GEORGE W. KISKER, J. Nerv. & Ment. Dis. **99**:343 (April) 1944.

The operation of prefrontal lobotomy or leukotomy provides a unique opportunity to study the behavioral changes in a large number of subjects after the production of a relatively exact lesion. Twenty patients on whom the operation had been carried out were studied by the author from the viewpoint of the relations existing between the prefrontal association areas and the diencephalon and the autonomic representation in the cortex.

On the basis of retrograde degeneration after cortical ablations, Walker concluded that the thalamus can conveniently be divided into three nuclear groups: The first group has exclusively subcortical connections; the second receives fibers from the ascending sensory tracts and sends efferent fibers to the cortical projection areas, and the third receives no ascending fibers but makes numerous connections with the thalamic nuclei of the second group and projects to the cortical associative areas. The thalamus is viewed as a subcortical center where incoming impulses are integrated to some degree.

There is considerable evidence for autonomic representation in the frontal cortex, the cortical influence being primarily inhibitory. Thus, section of the frontal lobes should decrease autonomic inhibition; the validity of this assumption was borne out by the behavioral changes in the patients, who displayed increased hunger, sphincter disturbances, dysfunction of the temperature control mechanism, nausea and vomiting, decreased anxiety and tension and somnolence. The last symptom is especially interesting in view of the great weight of evidence in favor of a center for waking and sleeping in the hypothalamus and the demonstrated neural pathways connecting the frontal poles and the hypothalamic complex.

The therapeutic effect of the operation may be due to interruption of the corticothalamic tracts and the consequent modification of affectointellectual relations. It is well established that there are direct tracts connecting the prefrontal lobe with the medial thalamic nuclei. These fibers make up the anterior thalamic radiation and bear the brunt of the damage in lobotomy. However, the cerebropontile connections from the frontal lobes to the nuclei of the pons are also probably affected, and there are tracts indirectly connecting the frontal lobes and the cerebellum. It is thus possible to visualize an intellectual-affective-motor chain which includes the prefrontal association areas, the medial thalamic nuclei, the cerebellum, the pons and tracts returning once again to the frontal lobes. The disruption of this chain by lobotomy leads to interference with affective patternization and to a concomitant

restructuralization of the motorium, which accounts for the therapeutic effects of the procedure.

CHODOFF, Langley Field, Va.

BIOCHEMICAL COMPONENT OF THE MANIC DEPRESSIVE PSYCHOSIS. PERRY C. BAIRD, J. Nerv. & Ment. Dis. **99**:359 (April) 1944.

The manic phase of manic-depressive psychoses has been considered to have some relation to overfunction of the adrenal gland. To investigate this concept, Baird injected whole blood from manic patients into adrenalectomized cats and compared these animals with respect to behavior and duration of life with a group of control adrenalectomized animals which received whole blood from normal subjects. The average duration of life following adrenalectomy in the cats receiving blood from the manic patients was eleven and a half days for 4 cats and ten and one-third days for 7 cats. In contrast, the 7 control cats receiving normal blood lived an average of four days. It was observed that 2 of the adrenalectomized cats receiving blood from manic patients displayed unusual strength and endurance, and 1 of them exhibited dramatic rage reactions despite the absence of adrenal glands. Two adrenalectomized rats receiving blood from manic patients lived eight times as long as 3 adrenalectomized rats receiving whole blood from normal persons. In one experiment a transfusion of 500 cc. of citrated whole blood from a manic patient had no effect on a patient in a deep depression.

The author suggests that the manic psychosis may be due to overstimulation of the entire autonomic nervous system, with consequent increase in the nerve impulses to the anterior lobe of the pituitary gland, from which a reservoir of hormones break loose. These enter the circulation and bring about a tremendous increase in the secretions of the thyroid, adrenals and gonads, which, in turn, are responsible for many of the symptoms of the manic state, such as excessive sexual drive and quick recovery from fatigue.

CHODOFF, Langley Field, Va.

REFERRED HEAD PAIN AND ITS CONCOMITANTS. DOUGLAS G. CAMPBELL and CLARE M. PARSONS, J. Nerv. & Ment. Dis. **99**:544 (May) 1944.

In order to investigate the nature and varieties of referred head pain, the mesodermal structures of the cervical and basioccipital somites of a number of volunteer subjects were irritated by scratching the periosteum and periarticular structures with a fine needle or by the injection of 6 per cent sodium chloride in sterile solution. It was found that irritation of structures in the region of the occipitoatlantal condyle and the first cervical interspace posteriorly caused referred pain, which was predominantly orbital and frontal from the condylar or basal region and predominantly occipital from the nuchal tissues. Pain originating from the cervical interspinous ligaments (second to fifth) was predominantly occipital and upper cervical, with only occasional frontal reference. Concomitants of giddiness, pallor, sweating and nausea were seen with basal, suboccipital and interspinous irritation. These symptoms varied in intensity, extent and duration. Infiltration of trigger spots with procaine was uniformly successful in temporarily relieving heterotopic pain and usually ameliorated the concomitant symptoms. The resemblance of the subjective states produced to the post-traumatic "head" syndrome and to certain "neuralgias" and "myalgias" of the occipitocervical region was notable.

The type of pain produced in these experiments is referred to as sclerotomal, as differentiated from the dermatomal pain produced from somites below the fifth cervical segment.

The production of head pain from disease of the cervical, thoracic, and even lumbosacral, portions of the spine is explained as being due to hypertension of the long axial back muscles, with traction on their collagenous attachments to the occipital portion of the cranium.

Sensory impulses from the deep suboccipital muscles reach the upper two cervical segments of the spinal cord and here may become associated synaptically with the spinal tract and nucleus of the fifth nerve. This suggests a mechanism whereby irritation of the suboccipital structures can account for anterior head pain.

Also, the close functional interplay between the muscles of the eyes and the posterior cervical muscles provides an explanation for the equilibratory disturbances seen in cases of the post-traumatic syndrome in which deep nuchol pain and spasm of cervical muscles are prominent features. Muscle spasm, whatever its cause, can provide the starting point for a vicious cycle because the pain produced gives rise reflexly to further spasm. In patients suffering from tension and anxiety states the production of such a vicious cycle, with spasm of the cervical muscles leading to head pain and further spasm, is the probable mechanism of the headaches so frequently seen and described as functional.

CHODOFF, Langley Field, Va.

ON GENUINE EPILEPSY. RALPH R. GREENSON, Psychoanalyt. Quart. **13**:139, 1944.

Greenson believes that, in addition to a hereditary predisposition on an organic basis, a psychologic predisposition to genuine epilepsy exists. He presents data obtained from the partial analysis of a man aged 20 with epilepsy. The analysis revealed that the patient had strong aggressive, hostile and criminal drives, passive homosexual longings and exhibitionistic, scoptophilic impulses. These trends were present partly as reaction formations and partly as direct expressions of instinct. The patient had a strong tendency to accumulate tensions instead of discharging small quantities, to block motor outlets and to shift excitation to the central nervous system.

The aura was an anxiety equivalent and an orgasm derivative. In the seizures fantasies appeared containing castration ideas and allusions to incestuous wishes. Murderous, sadistic and destructive drives were fantasied in the preconvulsive and postconvulsive states.

The first attack was precipitated by a stimulus which was associated with infantile repressed material. Later attacks were precipitated by similar stimuli and by all situations which increased internal tensions—anxiety, sexual excitement or rage. The greatest obstacle in the analysis was the inability to analyze successfully the passive, homosexual aspects of the transference.

Greenson believes that the psychologic predisposition to genuine epilepsy consists in the presence of strong anal sadistic trends. All psychologic stimuli which increase internal tensions, especially those which touch on a repressed infantile nucleus, may precipitate an attack. The seizure itself is a trauma and is reacted to with phobic mechanisms. The attack also may be felt as a punishment. The seizures may permit the discharge of hitherto repressed fantasies.

The author believes that his case could be classified as one of pregenital conversion hysteria.

PEARSON, Philadelphia.

THE GUARDHOUSE INMATE, WITH A BRIEF DESCRIPTION OF THE "PSYCHOPATHIC PERSONALITY." WILLIAM ROTTERSMAN, War Med. **5**:271 (May) 1944.

Rottersman studied 50 unselected inmates of a post stockade, using the Harrower-Erickson multiple choice (Rorschach) test, the Shipley-Hartford Retreat test, a questionnaire covering information about the family history, age, education, length of service, conflicts with the law, childhood behavior disorders, psychotic trends and psychoneurotic complaints, sick call tendencies and breaches of military discipline and a personal interview. He found that approximately one third of the prisoners could be labeled pronounced psychopaths. The remaining two thirds were borderline psychopaths, persons of abnormal intelligence and persons with mental disease. Of the whole group, only 10 to 20 per cent could be considered normal.

The author believes that the majority of guardhouse prisoners should never have been inducted, but since they are in the service, they should not be returned to civilian life because of the harmful effect on the morale of the reliable, conscientious soldiers and their relatives. Some might be sent to "labor" battalions; some require institutionalization, and some might profit from psychotherapy or chemotherapy.

PEARSON, Philadelphia.

SUGGESTIBILITY AND HYSTERIA. H. J. EYSENCK, J. Neurol. & Psychiat. **6**:22 (Jan.-April) 1943.

Eysenck investigated the phenomenon of suggestibility in 60 subjects, 30 of whom were hysterical and 30 nonhysterical men and women. He used the progressive weights and lines tests, involving both personal ("prestige") and impersonal ("nonprestige") suggestion; the body sway test; the arm levitation test, and the Chevreul pendulum test, as well as tests for intelligence, perseveration and personal tempo. In none of the tests of suggestibility were there significant differences between the hysterical and the nonhysterical subjects or between men and women. Thus, although hysterical persons are suggestible, they are not more so than nonhysterical persons. The tests used involved two types of suggestibility—primary and secondary. Primary suggestibility was distributed in the experimental population in the shape of a U curve, showed high reliability, was correlated with intelligence in a nonlinear manner (i. e., subjects of average intelligence were the most suggestible) and was shown to involve a type factor dividing suggestibility into the active and the passive type. Secondary suggestibility was distributed in the shape of a normal curve, showed a low reliability and was correlated with intelligence in a linear manner; i. e., the more intelligent the subject, the less suggestible he was. Primary suggestibility seemed to be concerned with simpler tasks and was related to the phenomenon of dissociation, whereas secondary suggestibility dealt with more complex processes of judgment which would make dissociation difficult. Two factors of emotional response, viz., aptitude and attitude, were active in primary suggestibility. The personal tempo was negatively related to suggestibility, but perseveration did not show any definite relation to it.

MALAMUD, Ann Arbor, Mich.

Diseases of the Brain

MULTIPLE MENINGIOMAS. JOSEPH A. MUFSON and LEO M. DAVIDOFF, J. Neurosurg. **1**:43 (Jan.) 1944.

Multiple meningioma is so rare that in a series of 295 cases of intracranial meningioma (Cushing and Eisenhardt) there were only 3 instances of the condition. Likewise, it is only in rare cases that such multiple growths have been successfully removed. Mufson and Davidoff report the removal of multiple meningiomas in 2 cases.

In the first case ten meningiomas were removed in four successive operations over the course of three years. All the tumors were in the right hemicranium. Of interest is the notable transition in histologic form —from a benign psammomatous meningioma, obtained first, to a malignant tumor, removed at the last operation. In the second case two meningiomas of mixed type (benign) were removed at a single operation from the left hemicranium. In neither case were there any of the stigmas of Recklinghausen's disease.

WHITELEY, Philadelphia.

SPONTANEOUS VENTRICULAR RUPTURE IN HYDROCEPHALUS WITH SUBTENTORIAL CYST FORMATION. J. PENNYBACKER and D. S. RUSSELL, J. Neurol. & Psychiat. **6**:38 (Jan.-April) 1943.

Pennybacker and Russell report 2 cases of hydrocephalus resulting from obstruction of the aqueduct in which the dilatation of the lateral ventricles was accompanied by rupture of their walls in the region of the vestibule, producing a subtentorial cyst which communicated with the lateral ventricle. The site of rupture was that part of the ventricle wall which is thinnest normally, i. e., in the medial angle of the collateral trigone, between the forward-sweeping crus of the fornix and the forceps major. In a third case of hydrocephalus resulting from occlusion of the foramens in the fourth ventricle by adhesive arachnoiditis thinning occurred without rupture of this area of the wall of the lateral ventricle. Ventriculographic examination established the diagnosis. The treatment advocated by the authors is, first, the establishment of an opening in the anterior part of the third ventricle and, if this proves ineffective, a collapse of the cyst by the cerebellar approach.

MALAMUD, Ann Arbor, Mich.

Diseases of the Spinal Cord

TRAUMATIC SPINAL ARACHNOIDITIS: REPORT OF TWO CASES. LEOPOLDO SALAZAR VINIEGRA, Arch. de neurol. y psiquiat. de Mexico **6**:127 (March-April) 1943.

Salazar Viniegra reports 2 cases of injury to the back, 1 in a woman aged 38 and the other in a man aged 30. In both cases there were periods of freedom from complaints of two and six months respectively. In both cases the appearance of severe weakness and sensory changes in the lower limbs was rapid (two and four days respectively after onset of complaints). The passage of iodized poppyseed oil was stopped, but without the typical diffuse arrest of droplets. In 1 case only 1 cc. of spinal fluid was obtained, and in the other none could be withdrawn. There was an increase in cells and protein in the spinal fluid. No manometric studies are recorded. In 1 case the Kahn reaction of the blood was positive, a finding which the author considers coincidental. The diagnoses of leptomeningeal

adhesions in 1 case and of a meningeal cyst in the other were verified by operation. No histologic studies were reported. The author assumes a definite relation between the trauma to the back and the development of adhesive arachnoiditis. SAVITSKY, New York.

Peripheral and Cranial Nerves

PAIN REFERRED TO THE FACE, NECK, UPPER EXTREMITY AND CHEST DUE TO LESIONS IN THE EAR. HENRY P. SCHUGT, Arch. Otolaryng. **39**:430 (May) 1944.

Schugt reports 2 cases of chronic mastoiditis in adult women in which pain was referred to the face, neck, upper part of the arm and thorax. In the first case radical mastoidectomy had been done on the right side several years ago. At that time a cholesteatoma was observed in the mastoid antrum and middle ear, with extensive destruction of the bone, including the facial canal. Ten years later the wound began to discharge, after an infection of the upper respiratory tract. There was associated pain in the ear, and the patient was rehospitalized. Neurologic examination revealed nothing abnormal. A revision of the mastoid cavity revealed a small cholesteatoma near the opening of the eustachian tube. During the postoperative course it was observed that pain was initiated when the anterior wall of the mastoid cavity or when the eustachian tube was touched or packed with a thin tampon. The pain spread instantly over the entire auricle to the face, the eye, the temple, the upper and lower lip, the neck, the upper part of the arm and the upper and lateral part of the chest. The pain responded only to strong sedatives and to local applications of a 10 per cent solution of cocaine. A second revision of the mastoid cavity revealed no further pathologic process. The pain, however, recurred in the same manner as after the first revision. Gradually complete epithelization took place, and the pain subsided.

In the second case, pain developed in the ear, in the upper part of the arm and the upper part of the thorax. It was less violent than in the first case and was not felt below the fourth rib. There was no evidence of local tenderness in the arm or chest. After a modified radical mastoidectomy, the pain subsided and was not present during the postoperative period, as in the first case. The author points out that as the site of the lesion in the first case was within the distribution of the trigeminal nerve, the pain felt in the temple and face may be considered as referred pain, conforming with Head's theory. The same holds true for the pain in the upper cervical region and the upper part of the arm, as the trigeminospinal tract reaches the level of the upper cervical nerves. The thoracic pain is explained by the fact that impulses arising at the site of the lesion reach the upper thoracic segments of the spinal cord through afferent spinal nerve components which traverse the plexuses on the common and internal carotid arteries.

RYAN, Medical Corps, Army of the United States.

EROSION OF THE ALA NASI FOLLOWING TRIGEMINAL DENERVATION. J. SCHORSTEIN, J. Neurol. & Psychiat. **6**:46 (Jan.-April) 1943.

Schorstein draws attention to a new syndrome which he observed in 8 cases following trigeminal denervation either by section of the nerve or after injection of alcohol into the gasserian ganglion. In the resulting anesthetic area of the face erosion of the ala nasi occurred and was frequently associated with paresthesias, self-inflicted trauma, epistaxis, nasal fissures and facial ulcer. The author is of the opinion that erosion of the nostril results from self-inflicted injury in an attempt by the patient to relieve himself of paresthesia. A contributing factor is the diminished resistance of anesthetic skin to superimposed infection. The progression of the lesions may be determined by failure of the cutaneous vasodilator reflex. Treatment consists of warning the patients against manipulation of the skin and of covering ulcers and fissures with a bland ointment. MALAMUD, Ann Arbor, Mich.

Treatment, Neurosurgery

THE PICROTOXIN TREATMENT OF BARBITURATE POISONING. JOSEPH F. DORSEY, J. Nerv. & Ment. Dis. **99**: 367 (April) 1944.

Owing to the increasing use of the barbiturate drugs in suicidal attempts, the recognition and treatment of barbiturate poisoning has assumed considerable importance. In cases of severe intoxications, with coma impending or present, active, and at times heroic, treatment is required. The patient should be placed in shock position and gastric lavage instituted immediately. Specific treatment is based on the intravenous use of picrotoxin in an amount dependent on the depth of coma. The drug is injected at the rate of 1 cc. (3 mg.) per minute until the appearance of tremors of the extremities, twitching of the lips and eyelids and movements of the eyes. When this stage is reached, the frequency of administration of the dose is decreased to keep the patient at a level of minimal twitching, since at this point the cardiac and respiratory centers receive their maximal stimulation. Usually 1 cc. every five minutes is sufficient for this purpose, and with improvement this dose is gradually decreased. An overdose of picrotoxin may produce a convulsion. In addition to picrotoxin, application of heat, intravenous injection of fluids, administration of caffeine and sodium benzoate and, occasionally, inhalation of carbon dioxide and oxygen are indicated. If use of the picrotoxin is discontinued prematurely, the patient lapses again into deep coma.

CHODOFF, Langley Field, Va.

TREATMENT OF MENTAL DISEASE WITH ELECTRIC SHOCK. CESAR DELGADO, Rev. de neuro-psiquiat. **6**:263 (Sept.) 1943.

Electric shock therapy was used for the first time in Peru in January 1943. The author reports his results with 10 patients: 5 with schizophrenia, 2 with depressions, 1 with a manic state, 1 with a compulsive neurosis and 1 with psychoneurosis. Seven patients had complete remissions, and 3 showed notable improvement. There were no fractures. One patient incurred a readily reducible dislocation of the shoulder. All the patients with manic-depressive psychosis and 3 with schizophrenia had complete remissions. All the schizophrenic patients treated had been ill six months or less. No persistent mental sequelae were noted in any of the patients. SAVITSKY, New York.

Society Transactions

PHILADELPHIA PSYCHIATRIC SOCIETY

HAROLD D. PALMER, M.D., *President, in the Chair*

Regular Meeting, March 10, 1944

Excessive Androgen in the Female. DR. MARGARET DE RONDE, Norristown, Pa.

Two interesting cases of pronounced virilism in females receiving androgen therapy were observed. Neither patient exhibited any indication of aberration in psychosexual development, although there was present enormous excess of androgens. In both patients the changes toward virilism, although substantial, were reversible.

DISCUSSION

DR. N. W. WINKELMAN: It is not pleasant to see the male characteristics produced in the female by excessive androgen therapy, especially when one has oneself prescribed the treatment. It is consoling that the condition is a reversible process, as has been stated this evening and as is recorded in the literature. My associates and I had been treating female psychiatric patients with androgen, and we had noted the growth of hair, the change of voice and the other alterations described. We, too, have observed reversibility. I must confess that the first time I saw such changes I was profoundly shocked, but the male characteristics eventually disappeared, after several months. Not more than 225 mg. of androgen per month per patient is recommended.

DR. HAROLD D. PALMER: One of the interesting facts brought out by Dr. De Ronde is the apparent absence in these patients of a relationship between psychosexuality and the endocrine state. In both her cases excess of androgen was continuous over a period sufficient to produce physical changes tending toward masculinity, and yet there was no parallel change in psychosexual interest. This observation becomes important with respect to the relation of hormone secretion and sexuality, not only with the normal, but in cases of sex variants. My associates and I, as well as other investigators, have shown that a high percentage of homosexual males excrete excesses of estrogen in the urine. It has been thought that administration of testosterone and other forms of androgen might conceivably inhibit the secretion of estrogen and might tend to produce a regression of feminine physical characteristics and a change toward normal psychosexuality. It seems to me that one will have to accept in part the concept that in some instances homosexuality is a neurosis, but that in others it is a psychobiologic entity and is, therefore, amenable to changes in the endocrine balance. I believe this theory would find a good deal of support in the glandular effects of treatment of homosexual males with large doses of testosterone. While we do not yet have any statistical statement to make, it has been our experience that in some cases normal psychosexuality develops after prolonged and intensive glandular therapy.

Psychiatric Experience on a Naval Hospital Ship. Lieut. R. S. WIGTON (MC), U.S.N.R.

Duty on a hospital ship combines the advantages of sea duty with those of working in a small, excellently equipped hospital unit and offers a varied and busy experience.

Of particular interest to the psychiatrist are the opportunities to see psychiatric battle casualties at an early stage, to compare the reactions of the men from varying types of duty and to be in close contact with wounded and medically ill men—caring for burns and treating medical or surgical casualties when conditions required.

In the care and transportation of the wounded and ill during the campaign at Guadalcanal, the high morale, patience and fortitude of these men were inspiring to see. During this campaign, 671 neuropsychiatric patients were handled, of whom 10 per cent were psychotic, slightly less than 50 per cent had the cardinal symptoms of "combat fatigue" and 25 per cent had various psychoneurotic reactions similar to those seen in civilian life.

The cruise of a year and a half provided an opportunity for observations on the reactions of the ship's crew to prolonged sea duty and to morale factors generally. A few of the original members of the crew, who had been out for over two years, presented reactions similar enough to constitute a syndrome, with symptoms of anorexia, insomnia, increased irritability and fears of their own impulsive action. These symptoms were not severe and were superficial.

Another group of men from the first showed chronic psychoneurotic reaction patterns, with episodes of psychosomatic symptoms, anxiety and mild depression. As a group their symptoms, personalities and basic problems were fairly similar. They responded well to ordinary psychotherapy and were of chief interest in that they reacted well to prolonged sea duty.

DISCUSSION

DR. T. L. DEHNE: Lieutenant Wigton mentioned the development of a chronic combat fatigue pattern. Is that too variable to describe, or could he present it in a few words? Do patients with combat fatigue look like civilian patients in chronic neurotic states? What is the prognosis for these patients? Do patients with combat fatigue go back to duty, and do they stand up well after their return?

Lieut. R. S. WIGTON (MC), U.S.N.R.: My colleagues and I used sedatives freely as needed, to assure adequate sleep and freedom from disturbing symptoms. Prolonged narcosis was not employed as the patients did not usually remain for extended periods. Narcosis treatment of patients with combat fatigue was limited by factors of time and numbers and was not often needed for control of disturbing symptoms. These usually subsided within a day or two. We felt that the patients were greatly aided by quiet surroundings, good food, hot showers and comfortable beds, as well as by interviews which gave them an opportunity to relate their experiences and to obtain relief from their tendency to self criticism and feelings of guilt through reassurance and explanation. The understanding and helpful attitude of the personnel of the ship as a whole was of great value. Chronic neurotic states were seen which were analogous to civilian neuroses. The combat fatigue syndrome developing in men without discernible predisposition differed clinically. In speaking of a more chronic combat fatigue reaction, I refer to the men who, after losing their acute dramatic symptoms, need further

treatment and rest for persisting startle reactions, impairment of self confidence and increased anxiety reactions to situations of stress.

We did not have the advantage of long observation of these patients and do not have first hand information concerning the further course of their illness. It is to be expected that their symptoms will gradually subside. More prolonged reactions are analogous to chronic anxiety states in civilian life.

Present Day Trends in Psychiatry. DR. KENNETH E. APPEL.

A number of cases from World War I, some from World War II and a civilian case were presented, to show what goes on in the therapeutic process of psychiatric disorders. In World War I, it was found that shell shock was not due to organic injury to the nervous system—the causes were factors of which the patient was unaware. Hypnosis was used in some cases. Rivers expressed the opinion that the patient should recognize and assimilate his terrifying experiences, and he was encouraged to do this in ordinary conversation. Consideration and understanding, rest and sympathy were found to be more important than intellectual formulation or explanation.

In World War II, a similar method is employed—a state of partial sleep is induced by the intravenous use of pentothal sodium. In this state the patient will talk of his experiences and express his fears or resentment, and with repeated use of this procedure he is relieved of his malignant tensions and in many cases can return to his company.

In the case from civilian life, a man, because of his early training, had become a perfectionist, and fear, hate and resentment had led to physical illness with bleeding ulcers, for which medical therapy was of no avail. Feelings of resentment and antagonism were allowed to well up in psychiatric interviews, and the ulcers healed and the fears disappeared. Many such patients recover after the recalling of forgotten events and the expression of intense emotion, without the development of insight. So one need not make therapeutic efforts too intellectual or consider insight as a criterion of recovery. Patients get a sense of security, protection, support and understanding on the part of the physician, and these factors are more important than specific drugs, reasoning and explanation.

DISCUSSION

DR. J. C. YASKIN: I am in agreement with Dr. Appel that psychotherapy for the majority of patients is a rational scientific procedure. Most patients, however, recover not because they obtain insight but, I believe, in spite of it, and most of the time without any intellectual insight. I am yet unable to form a clear idea of the mechanism by which the psychoneurotic patient improves with psychotherapy, but I believe the principles indicated by Dr. Appel apply to the majority of patients. I cannot escape the conclusion that in the everyday practice of psychotherapy suggestion and reassurance are important factors. The first value of the psychotherapeutic approach which Dr. Appel outlined rests on the fact that one can carry on for many hours without exhausting useful material, obtainable only through free association.

The treatment of patients with war neuroses should be somewhat modified. Such persons may be divided into two groups: patients destined to be psychoneurotic by prewar makeup and persons who become neurotic by reason of the hardships of war. The distinction is just as clear in this situation as it is in civilian life, in which two types of psychoneurotic patients are recognized; persons who have a psychoneurotic makeup of long standing, which emerges with some precipitating factor, and persons with true neuroses whose personalities are fairly well integrated. The psychoneurotic patient with a defective personality background reacts in large measure in war as he does in civilian life. With the patient suffering from a war neurosis the situation is different, since under stress of war conditions he acquires a so-called fatigue neurosis, which is practically equivalent to the problem of an acute anxiety neurosis in civilian life. Men with such a condition react satisfactorily with one treatment or another. In World War I many patients presented pure conversion symptoms. There were hundreds of men and officers with paralyzed legs who had no anxiety and were enjoying their situation. I saw hundreds get well on Nov. 11, 1918 who were not suffering from an acute anxiety state. With these men hypnosis, persuasion and good old-fashioned suggestion and shock were useful. Corpsmen were taught that when a new train arrived they were to tell the men they would get well in a few weeks, and it worked. Patients recovered in a matter of weeks, instead of months. Suggestion is an important mode of approach with some patients with these neuroses, but not with those who have severe anxiety.

Suggestion should still play a major role in the treatment of some neuroses in the war situation, even as it does in the physician's office, and I dare say patients are encountered for whom deep psychotherapy is not advantageous. Some patients with hysterical aphonias or paralyses react better to suggestion than to deep analysis. With some of these patients profound analysis is not conducive to therapeutic results.

DR. S. B. HADDEN: I appreciate Dr. Appel's presentation of this method of approach to the neurotic states, but I wish to express my disagreement with his comment that real cure can occur without development of insight. Dr. Appel and I may be speaking of the same thing from different points of view. I am sure that he does not refer to an intellectual type of insight—one with complete understanding of all mental mechanisms; I do not believe that that type of insight is necessary for cure, but I do feel that insight and understanding of the nature of behavior are necessary to recovery and that in Dr. Appel's case this occurred. By the free passive type of analysis, the patient is stirred to a voluble discussion of his early life, and his repressions and feelings of hostility may be verbalized; as this goes on, he gradually acquires a degree of emotional insight. As the result of emotional, rather than of intellectual, insight there is a more satisfactory appreciation and adjustment of his personality difficulties. Many times the patient does not know why he got well, but he was brought through an experience that gave him emotional, and not intellectual, insight. It is also important that many incidents that are most valuable in therapy the physician may not consider important at all. I am sure every one is interested to know why one does succeed in some cases. I had a rather dramatic experience of this kind with a minister of a very rigid sect. We had had several unsatisfactory interviews. One day he said, "Doctor, I should think that you, knowing that I am a minister and that I am opposed to smoking, would refrain from smoking in my presence." I said, "Why should I?" He was upset by my response but continued treatment. After he reached a certain point in the road to recovery, he said, "Doctor, I feel that I am getting better, but I thought I would

never improve under your care." I asked, "Why do you suppose you are getting better?" He answered, "You sort of burst my bubble. The day that you did not stand in awe of me, a minister, did something to me." My remark was certainly not a planned procedure, but it helped him to acquire insight into the fact that he was utilizing his ministry to cloak certain inadequacies.

I think that many times we psychiatrists lead patients through a passive analysis which does not give them understanding, or, as we call it, insight, but they have acquired a subconscious, an emotional, insight, which in my opinion is better than the intellectual insight. Many patients obtain real intellectualized insight which is of no use to them.

DR. F. H. LEAVITT: These cases are quite similar to those that I had while with the American Expeditionary Forces in France, in 1918. For such men as these, there were three neurologic field hospitals and, back of these, two neurologic base hospitals. It was found in the field hospitals, where the psychiatric patients were received early, and within a few miles of the front line area, that from 75 to 90 per cent of them could be returned to duty within about seven days. The majority of these patients were then said to have "shell shock," but at present the condition is termed "battle fatigue." There were also a number of patients with conversion hysteria, and success with them was variable. A regimen of regular feeding, sleep and psychotherapy did wonders to get these men back to duty; for the men who did not improve or get well within a reasonable time the prognosis was bad, and many of them were seen years later at the Veterans Administration Facility and at government hospitals.

Memorial to Dr. Charles W. Burr. DR. F. H. LEAVITT.

Dr. Charles W. Burr died on Feb. 19, 1944, at the age of 82 years. Dr. Burr was one of the founders of the Philadelphia Psychiatric Society and was president on three occasions. He was past president of the American Neurological Association and past president of the Pathological Society of Philadelphia. He served as professor of mental diseases at the University of Pennsylvania Medical School from 1901 to 1930 and was emeritus professor of mental diseases from 1931 to 1942.

PHILADELPHIA NEUROLOGICAL SOCIETY

GEORGE D. GAMMON, M.D., *Presiding*

Regular Meeting, Feb. 25, 1944

Meningioma of the Lateral Ventricle: Report of a Case. DR. FRANCIS C. GRANT.

A white man aged 42 was admitted to the University Hospital on April 29, 1942, complaining of headache, ataxia, convulsions and fatigue. Because of interstitial keratitis he had been treated for syphilis for many years. Nine years prior to admission he noted that he staggered when he walked and began to have headache. Eight years before admission deafness developed. Five months prior to admission he noted tremor and weakness of the right hand, his headache became more severe and he staggered easily. Two weeks before admission he had a generalized convulsion, ushered in by a feeling of dizziness.

The positive neurologic findings were bilateral deafness, more pronounced on the left side; irregular, sluggish pupils; ataxic gait, and a questionable Babinski sign on the left side. The eyegrounds and visual fields were normal.

Roentgenographic studies of the head revealed nothing abnormal.

Air studies showed a complete block of the right ventricle, and the exploring needle demonstrated a resistant mass in this area.

Through a right temporoparietal bone flap and cortical incision, a purplish, discrete tumor, trilobular and forming a cast of the ventricles, was easily and completely removed. No attachment to the choroid plexus was noted. The tumor weighed 75 Gm.

Microscopic examination showed that the tumor was a fibroblastoma of the arachnoid.

Postoperative convalescence was smooth. The patient returned to work in six months and has had no further symptoms to date.

DISCUSSION

DR. N. W. WINKELMAN: I treated this man many years ago for neurosyphilis. At that time he had the interstitial keratitis and the deafness which he still manifests. I lost track of him about four or five years ago. I congratulate Dr. Grant on a brilliant diagnosis and surgical procedure.

The Scalenus Anticus Syndrome. DR. BERNARD D. JUDOVICH.

The scalenus anticus syndrome may be primary or secondary, the former usually being due to trauma and the latter associated with local lesions, such as tendonitis, bursitis or myositis.

A spastic scalene muscle may compress the subclavian artery, which lies in the acute angle formed by the muscle and the first rib. In rare instances an anomalous subclavian vein may be compressed. Tenderness of nerve pattern type may occasionally be encountered.

The symptoms, which consist of pain, numbness and a sensation of heaviness in the arm, tenderness, paresthesias and coldness of the hand, are correlated with the anatomic structures affected. In 1 case the pain of angina pectoris was simulated. In 2 cases compression of the subclavian vein simulated arthritis of the hand. In another case vasomotor instability simulated Raynaud's disease.

Diagnostic procedures include demonstration of tension and compression of the scalenus muscle; oscillometric dynamometric and cutaneous temperature readings, and the procaine test.

A new method of infiltration of the muscle with injection of procaine hydrochloride for diagnostic and therapeutic purposes is discussed. Factors which may cause a false interpretation of the test are a Horner syndrome and peripheral anesthesia following the injection of procaine. If either of these signs is present after injection, the test should be disregarded and the procedure repeated on another occasion.

Treatment includes repeated infiltrations of procaine, postural correction and surgical measures.

This paper was published in full in another journal (Judovich, B.; Bates, W., and Drayton, W., Jr.: *Am. J. Surg.* **63**:377 [March] 1944).

DISCUSSION

DR. H. E. YASKIN: If one observes a patient holding his hand over his head, with a sad expression on his face, one may anticipate cure by attack on the scalene muscle. Failure in some cases may be due to one of several factors, among which the functional element must play a major role. A neurotic patient may have localized pain. This is one source of therapeutic disappointment. Does Dr. Judovich have the number of patients he has actually treated?

DR. BERNARD D. JUDOVICH: The number of patients actually treated was over 100, and of these a number were relieved. Since my colleagues and I have changed our technic of injections we have had a high percentage of good results.

In the case presentered here there was no evidence of intraspinal lesion. Dr. Grant was not inclined to proceed with subarachnoid studies, and I feel that he was correct. Discoloration of the hand with involvement of three fingers in a patient who tends to carry his arm over the head points to an easy diagnosis, and the result of treatment is usually satisfactory. Our patients are treated with two or three injections of procaine. An occasional patient gets well without injections, and 1 patient in our group recovered with physical therapy, exercises and application of diathermy to the supraclavicular region. A diagnosis of compression of the scalene muscle does not always mean an operative procedure.

DR. GEORGE D. GAMMON: I should like to ask about the pain mechanisms involved in cases of this syndrome. I was glad to see that the author differentiated the relief obtained with infiltration of the muscle directly from relief obtained with production of the Horner syndrome and of anesthesia in the brachial plexus.

Dr. L. Kraeer Ferguson studied a similar group of patients at the university and reported to the section of neurology that the patient often did not get relief of pain unless he produced a Horner syndrome. Dr. Judovich is wise to separate the group who obtain relief from infiltration of the sympathetic fibers from patients who obtain relief from infiltration of the scalene muscle alone.

In another case, after injection into a section of scalenus muscle by Dr. Freeman, the patient was immediately relieved of her pain and did fairly well for two or three weeks. Suddenly there was a terrific attack of pain, lasting, I believe, from six to twelve hours, followed by weakness, with notable advance in atrophy in the muscles of the hand. It was as though there had been an interruption of the blood supply of the brachial plaxus. I wonder whether Dr. Judovich has had any similar experience.

Finally, I should like to ask what 2 cc. of procaine hydrochloride does to the muscle? Does it anesthetize the muscle itself? What evidence is there that it relaxes the muscle and relieves pressure? Would not the test of such an effect be a reverse procedure—injection of an irritating substance in the muscle, such as Lewis has done with a solution of sodium chloride, in order to see whether the pain was increased? It has been a question in my mind for some time just what the action of the procaine was, and I should like Dr. Judovich to comment on that, if he will. Is it necessary to infiltrate a muscle at the side of the entering nerve supply in order to obtain relaxation? Does it matter where the injection is made?

DR. BERNARD D. JUDOVICH: I do not know exactly what the procaine does except to paralyze the muscle temporarily, and this effect is palpable to the hand. The muscle is spastic before the injection and relaxed afterward. I believe it is tension against the vessel itself which causes pain. A good deal of pull would be needed to raise a patient's rib. We noticed, as I said, that we had operative failures in cases in which a Horner syndrome followed injection. We had a clue to this with a patient who showed a Horner syndrome after one injection and not after the other. She had relief with both infiltrations and was cured by operation.

We usually infiltrate the procaine at the lower end of the muscle, about 1 to 1½ inches (2.5 to 4 cm.) above the clavicle. The nerve supply comes from the third, fourth and fifth segments and sends branches into the muscle itself; I believe no nerves enter the lower end of the scalenus muscle.

DR. S. B. HADDEN: If Dr. Judovich had done nothing but call attention to the fact that in many cases of this syndrome the condition is secondary to some other painful lesion around the shoulders his presentation would still have been excellent, but he has done more. For the past seventeen years I have been associated with the police and fire department as consulting neurologist in the welfare department. Police and firemen are a breed unto themselves and have a large number of occupational diseases, this syndrome being one of them. I have reported before this society some of the curious disorders that policemen and firemen present. For example, a case of meralgia paresthetica is almost a daily occurrence, and the reason is apparent when I say that on several occasions I have weighed the pistol belt and pants of patrolmen and found them to weigh anywhere from 12 to 22 pounds (5.4 to 10 Kg.). In the course of the past seventeen years I have seen at least 200 cases of meralgia paresthetica. I have likewise seen a great number of cases of scalenus anticus syndrome. They are usually secondary to some other lesion around the shoulders, and the fact that certain policemen wear a shoulder holster, weighing from 7 to 10 pounds (3.2 to 4.5 Kg.), which swings on them at least eight hours a day is a factor. They come to me with myositis, or a painful shoulder if you will, and gradually secondary fixation, with contraction of the scalenus anticus muscle and this syndrome, is added. Many local conditions of the shoulder are associated with this condition, but almost inevitably there occur the elevation, fixation and secondary scalenus anticus syndrome. We have been giving injections in such cases, with surprisingly good results. We have discovered that there is not much use in injecting procaine into the scalenus anticus muscle alone and allowing other painful lesions around the shoulder joints to continue; these should be taken care of at the same time. Also, we have usually preceded and followed injection into the scalenus anticus muscle with the application of short wave diathermy and exercise. It is of the utmost importance, when the patient has been made free of this pain, to get him to exercise the painful shoulder, keeping it up for ten or fifteen minutes after the injection. I should say that our percentage of good results with that procedure has been about 75 or 80.

One must regard this syndrome as a secondary rather than as a primary disease, and it most often can be relieved without operation. Formerly a great many of our patrolmen were operated on, when it was fashionable to do so, but I believe that injection into the scalenus

anticus muscle for this and other painful lesions around the shoulder, combined with use of local heat and exercise, is giving relief in a much higher percentage of cases.

In how many cases did Dr. Judovich find the complication of occipital neuralgia? We have seen a great many such cases in the police department, for traffic policemen will stand on a windy corner for several hours, with their backs to the wind and coat collars turned up to protect their necks, and when seen will have occipital neuralgia, as well as all the classic symptoms of the scalenus anticus syndrome.

DR. BERNARD D. JUDOVICH: We find occipital neuralgia in about 15 per cent of our cases. We usually infiltrate the scalenus muscle; if the patient obtains relief from the occipital neuralgia nothing more is done. In other cases it may be necessary to infiltrate the occipital region.

DR. MICHAEL SCOTT: Perhaps the reason for the relief of the pain after injection of the scalenus anticus muscle is not the analgesia following the injection but, rather, the interruption by the anesthesia of the proprioceptive fibers in the muscle, resulting in loss of muscle tone, relaxation and therefore relief.

News and Comment

COURSE OF STUDY IN THE RORSCHACH TEST, MICHAEL REESE HOSPITAL

The course on the Rorschach test offered by Michael Reese Hospital, Chicago, is scheduled this year for the week of June 4 to 8 inclusive. The records to be demonstrated will be representative of the older adolescent and the younger adult, with especial emphasis on persons discharged from the military services. Dr. S. J. Beck, head of the psychology laboratory, will conduct the course. It meets twice daily, in two hour sessions. Interested persons may inquire of the secretary, Department of Neuropsychiatry, Michael Reese Hospital, 2908 Ellis Avenue, Chicago 16.

CANCELLATION OF MIDWEST CONFERENCE ON REHABILITATION

At the request of the War Committee on Conventions, Washington, D. C., the Institute of Medicine of Chicago has canceled its Midwest Conference on Rehabilitation, scheduled for Monday, February 12, at the Drake Hotel, Chicago.

Book Reviews

Crime and the Human Mind. By David Abrahamsen, M.D. Price, $3. Pp. 244. New York: Columbia University Press, 1944.

Inasmuch as there have been so few books written on the subject of crime in definite connection with psychiatry, any attempt to evaluate the conclusions derived therein must needs be guarded.

Statements in the preface would indicate that the author has had a rather enviable variety of experience, including work in criminology in Norway, association with the Illinois State Penitentiary and, lately, as a member of the staff of the Court of General Sessions, New York city.

The subject matter deals largely with a succinct and condensed review of the literature concerned with the criminologic, biologic, anthropologic and psychiatric (including the psychoanalytic) aspects of crime. The cultural and sociologic aspects also receive appraisal.

Having digested, or redigested, all of this material, one is still left with the main question unanswered, namely: What is the relationship between crime and psychiatry? As is admitted by the author, less than 10 per cent of criminal activity is accounted for by psychosis or mental deficiency. That criminals are deviates from the accepted average is axiomatic. Yet when one attempts to interpret the antisocial behavior of the criminal exclusively in terms of psychopathology, one almost invariably is obliged to fall back on conjecture. Aside from the psychotic and mentally defective personality, the author introduces a new classificatory label for the psychopath, namely, the neurotic character. As with the "compulsive psychoneurotics and psychasthenics," psychotherapy, or reeducation, is advised. Just how this recommendation is to be put into effect on any appreciable scale is not mentioned except through the author's allusion to the work being done in one or two dubious federal penal institutions. He does not go as far as Karpman and Zilboorg, who advocate prolonged psychotherapy in a mental institution for this group of offenders. He does strike a rather hopeful, though dubious, note, however, in averring that the psychopath, or his freshly substituted neurotic character, "provided no organic lesion is present, has a chance to mature and to adjust socially when [he reaches] forthy-five if properly provided with adequate institutional training."

In the final paragraphs, the author seems to grasp the crux of the situation when he states: "The behavior of the individual, be it a personal or a social maladjustment, is only a reflection of how disorganized society is." He fails to add, however, that these unhealthy cultural and educational influences have their origin in unhealthy concepts of parental and school training systems; otherwise, over 60 per cent of the offenders would not begin their criminal preoccupations during their period of exposure to these systems.

As to remedial measures, certainly individual psychotherapy, as administered in mental hygiene and court clinics and in prisons, has effected little, if any, diminution in the incidence of crime; nor have the indirect therapeutic methods, such as are utilized in the probation, parole and reformatory systems, brought about any appreciable abatement in criminal offenses.

It is to be hoped that the author may produce a supplementary volume analyzing these faulty training methods and therein make appropriate recommendation as to constructive alterations.

The book should be of assistance to the student of criminal psychiatry.

La oliva bulbar; estructura, función y patología. By J. O. Trelles. Pp. xi plus 105, with 46 illustrations. Lima, Peru: Editorial Lumen, 1944.

In this handsomely printed monograph, Trelles has summarized what is known about the inferior olive, much of it based on his own researches in Paris. It seems that much more is known of the anatomy and pathology of this prominent structure than of its function. However, new light has been shed on its function during the past decade, since the concurrence of olivary hypertrophy and palatal myoclonus has been established. This is shown in the 28 cases collected by the author. Concurrent lesions, however, have complicated the problem. In most cases of palatal myoclonus there have been lesions of the central tegmental fasciculus on the same side; but in a minority of cases the contralateral dentate nucleus has suffered, and in 1 case neither structure was affected. Moreover, not all lesions of the fasciculus or of the dentate nucleus are sufficiently severe to provoke the hypertrophy. When it occurs, the hypertrophic change may commence within a week of the exciting lesion and may last for years. The olivary hypertrophy not only is gross but includes the ganglion cells, which undergo extraordinary reduplication of processes and peculiar distortions, as shown by drawings and by photomicrographs. The author designates these changes as gigantocytosis with paraphytosis and compares the mechanism with that observed with certain lesions of peripheral neurons. He leans away from the transsynaptic degeneration theory, since he has shown a well defined connection between the dentate nucleus and the opposite olivary body by way of the superior cerebellar peduncle.

Preliminary chapters deal with the anatomy and connections of the olivary body and the developmental aspects through the vertebrate series and in the individual organism. Sclerosis of the olivary nucleus may occur in particularly prominent fashion in dementia paralytica, and may thus underlie the dysarthria of this disease. Senile changes in the olives are common, but senile plaques are not encountered. On the other hand, in myoclonus epilepsy the cells are always affected, sometimes in isolated fashion. Isolated degenerations of the olivary bodies occur rarely and are accompanied by rigidity and tremor. More frequently, the olives are involved together with the cerebellum and other structures in the well known system diseases. A good bibliography and author index complete the work. While it is apparent from this monograph that lesions of the olive are associated with disturbances in muscular function in the nature of myoclonias, tremor and rigidity, the function of the olives in assuring smooth and coordinated action of the various muscles still remains much of a mystery.